

EP04/11646

PCT/EP200 4 / 0 1 1 6 4 6



Europäisches
Patentamt

European
Patent Office

Office européen
des brevets

REC'D 23 NOV 2004

WIPO

PCT

Bescheinigung

Certificate

Attestation

Die angehefteten Unterla-
gen stimmen mit der
ursprünglich eingereichten
Fassung der auf dem näch-
sten Blatt bezeichneten
europäischen Patentanmel-
dung überein.

The attached documents
are exact copies of the
European patent application
described on the following
page, as originally filed.

Les documents fixés à
cette attestation sont
conformes à la version
initialement déposée de
la demande de brevet
européen spécifiée à la
page suivante.

Patentanmeldung Nr. Patent application No. Demande de brevet n°

03023581.6

PRIORITY

DOCUMENT

SUBMITTED OR TRANSMITTED IN
COMPLIANCE WITH RULE 17.1(a) OR (b)

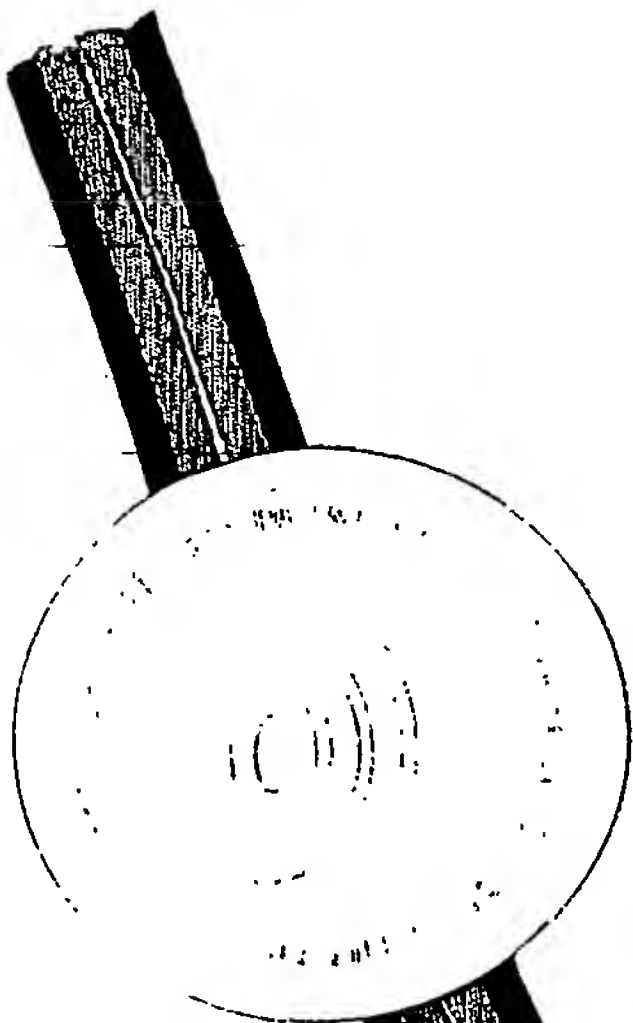
Best Available Copy

Der Präsident des Europäischen Patentamts;
Im Auftrag

For the President of the European Patent Office

Le Président de l'Office européen des brevets
p.o.

R C van Dijk





Anmeldung Nr:
Application no.: 03023581.6
Demande no:

Anmeldetag:
Date of filing: 16.10.03
Date de dépôt:

Anmelder/Applicant(s)/Demandeur(s):

Micromet AG
Staffelseestrasse 2
81477 München
ALLEMAGNE

Bezeichnung der Erfindung/Title of the invention/Titre de l'invention:
(Falls die Bezeichnung der Erfindung nicht angegeben ist, siehe Beschreibung.
If no title is shown please refer to the description.
Si aucun titre n'est indiqué se référer à la description.)

Multispecific deimmunized CD3-binders

In Anspruch genommene Priorität(en) / Priority(ies) claimed /Priorité(s)
revendiquée(s)
Staat/Tag/Aktenzeichen/State/Date/File no./Pays/Date/Numéro de dépôt:

Internationale Patentklassifikation/International Patent Classification/
Classification internationale des brevets:

C07K16/00

Am Anmeldetag benannte Vertragstaaten/Contracting states designated at date of
filing/Etats contractants désignées lors du dépôt:

AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LU MC NL
PT RO SE SI SK TR LI

5

Multispecific deimmunized CD3-binders

10 The present invention relates to a cytotoxically active CD3 specific binding construct comprising a first domain specifically binding to human CD3 and an Ig-derived second binding domain. Furthermore, a nucleic acid sequence encoding a CD3 specific binding construct of the invention is provided. Further aspects of the invention are vectors and host cells comprising said nucleic acid sequence, a process for the production of the construct of the invention and composition comprising said construct. The invention also provides the use of said constructs for
15 the preparation of pharmaceutical compositions for the treatment of particular diseases, a method for the treatment of particular diseases and a kit comprising the binding construct of the invention.

20 Human CD3 denotes an antigen which is expressed on T cells as part of the multimolecular T cell complex and which consists of three different chains: CD3- ϵ , CD3- δ and CD3- γ . Clustering of CD3 on T cells, e.g. by immobilized anti-CD3 antibodies leads to T cell activation similar to the engagement of the T cell receptor but independent of its clone-typical specificity; see WO 99/54440 or Hoffman (1985) J. Immunol. 135:5-8.

25

Antibodies which specifically recognize CD3 antigen are described in the prior art, e.g. in Traunecker, EMBO J 10 (1991), 3655-9 and Kipriyanov, Int. J. Cancer 77 (1998), 763-772. Lately, antibodies directed against CD3 have been proposed in the treatment of a variety of diseases. These antibodies or antibody constructs act as
30 either T-cell depleting agents or as mitogenic agents, as disclosed in EP 1 025 854. Human/rodent hybrid antibodies which specifically bind to the human CD3 antigen complex are disclosed in WO 00/05268 and are proposed as immunosuppressive agents, for example for the treatment of rejection episodes following the transplantation of the renal, septic and cardiac allografts. WO 03/04648 discloses a
35 bispecific antibody directed to CD3 and to an ovarian cancer antigen. Furthermore,

Kufer (1997) *Cancer Immunol Immunother* 45:193-7 relates to a bispecific antibody specific for CD3 and EpCAM for the therapy of minimal residual cancer.

However, prior art antibodies directed against CD3 are derived from non-human sources. This leads to several serious problems when using such anti-CD3 antibodies as part of a therapeutic regimen in humans.

One such problem is "cytokine release syndrome (CRS)". CRS is a clinical syndrome which has been observed following the administration of the first few doses of anti-CD3 antibodies and is related to the fact that many antibodies directed against CD3 are mitogenic. In vitro, mitogenic antibodies directed against CD3 induce T cell proliferation and cytokine production. In vivo this mitogenic activity leads to the large-scale release of cytokines, including many T cell-derived cytokines, within the initial hours after the first injection of antibody. The mitogenic capacity of CD3-specific antibodies is monocyte/macrophage dependent and it involves the production of IL-6 and IL-1 β by these cells.

CRS symptoms range from frequently reported mild "flu-like" symptoms to less frequently reported severe "shock-like" reactions (which may include cardiovascular and central nervous system manifestations). Symptoms include, inter alia, headache, tremor, nausea/vomiting, diarrhoea, abdominal pain, malaise and muscle/joint aches and pains, generalized weakness, cardiorespiratory events as well as neuropsychiatric events. Severe pulmonary oedema has occurred in patients with fluid overload and in those who appeared not to have a fluid overload. Another serious problem hampering the therapeutic use of, especially, murine monoclonal antibodies is the mounting of a humoral immune response against such antibodies, resulting in the production of human anti-mouse antibodies ("HAMAs") (Schroff (1985) *Cancer Res.* 45:879-885, Shawler (1985) *J. Immunol.* 135:1530-1535). HAMAs are typically generated during the second week of treatment with the murine antibody and neutralize the murine antibodies, thereby blocking their ability to bind to their intended target. The HAMA response can depend on the murine constant ("Fc") antibody regions or/and the nature of the murine variable ("V") regions.

The prior art contains various approaches to reducing or preventing the production of HAMAs by modifying monoclonal antibodies of non-human origin.

5 One approach to reducing the immunogenicity of such antibodies is by humanization, as for example described in WO 91/09968 and US 6,407,213. In general, humanization entails substitutions of non-human antibody sequences for corresponding human sequences, as for example is the case with CDR-grafting.

10 Another approach to reducing the immunogenicity of such antibodies is by deimmunization, as for example described in WO 92/10755, WO 00/34317, WO 98/52976, WO 02/079415, WO 02/012899 and WO 02/069232. In general, deimmunization entails carrying out substitutions of amino acids within potential T cell epitopes. In this way, the likelihood that a given sequence will give rise to T cell epitopes upon intracellular protein processing is reduced.

15

However, humanized and deimmunized antibodies often exhibit a decreased binding affinity with respect to their target as compared to their non-humanized parent antibodies and also often are still somewhat immunogenic in a human host.

20 Therefore, the technical problem of the present invention was the provision of means and methods for the treatment of and/or the amelioration of tumorous diseases, proliferative disorders as well as B-cell related diseases by induction of T cell mediated immune response. The above-mentioned means and methods should overcome the recited disadvantages of known antibody-based therapies.

25

The solution to said technical problem is achieved by providing the embodiments characterized in the claims.

30 Accordingly, the present invention relates to a cytotoxically active CD3 specific binding construct comprising a first domain specifically binding to human CD3 and an Ig-derived second binding domain,

wherein said first domain is deimmunized and comprises a CDR-H1 region, a CDR-H2 region and a CDR-H3 region, said CDR-H3 region comprising an amino acid sequence as depicted in SEQ ID NO 96, 108, 119, 120, 121, 122, 123, 124, 125,

126, or 127; and

wherein said first domain further comprises in its framework H1 the sequence VKK (Val-Lys-Lys) and wherein the transition sequence between framework H1 and CDR-H1 region comprises the sequence Ala-Ser-Gly-Tyr-Thr-Phe (ASGYTF; SEQ ID NO: 233).

It was surprisingly found that the above-recited, specific modifications to known CDR regions as well as framework regions and their corresponding transition sequences lead to deimmunized, CD3 specific binding molecules which show reduced immunogenicity but retain their cytotoxic activity compared to original non-deimmunized sequences. This finding was in particular surprising since not all possible deimmunization protocols led to bioactive, functional constructs which show distinct cytotoxic activity; see appended examples. Furthermore, surprisingly the deimmunized cytotoxically active CD3 binding molecules showed increased productivity. In accordance with this invention, specific sequences of non-deimmunized antibodies have been replaced by/modified to the sequences recited here above. In particular, in framework H1 regions original sequence Leu-Ala-Arg (LAR) has been replaced by the sequence Val-Lys-Lys (VKK). Furthermore, the sequence Thr-Ser-Gly-Tyr-Thr-Phe (TSGYTF) comprised in the transition region of framework H1 and CDR-H1 of some non-modified/non-deimmunized CD3-specific antibodies has been modified in accordance with the invention to Ala-Ser-Gly-Tyr-Thr-Phe (ASGYTF) (SEQ ID NO.:233) (see Figure 14). A desired, inventive CD3-specific binding construct is characterized as comprising at least two binding specificities whereby a second binding specificity is Ig-derived. Furthermore, said desired constructs are characterized by the specific amino acid sequences shown herein above. As documented in the appended examples the constructs as provided herein still retain bioactivity in their modified/deimmunized form. The examples also document that not all deimmunizations, determined by methods known in the art (WO 92/10755, WO 00/34317, WO 98/52976, WO 02/079415 or WO 02/012899), lead to bioactive molecules; see in particular the examples 2 and 5.

The term "cytotoxically active CD3 binding construct" as used herein relates to a CD3 specific construct capable of binding to human CD3 complex expressed on T cells and capable of inducing elimination/lysis of target cells. Binding of CD3 specific

binders of the CD3/CD3 complex (e.g. antibodies, antibody derivatives or antibody fragments) leads to activation of T cells as known in the art; see WO 99/54440. Accordingly, an inventive construct has to be able to eliminate/lyse target cells in vivo and/or in vitro. Corresponding target cells comprise cells expressing a surface molecule, which is recognized by the second Ig-derived binding domain of the inventive constructs. Such surface molecules are characterized herein below.

Cytotoxicity can be detected by methods known in the art and methods as illustrated herein below and in the appended examples. Accordingly, such methods comprise, inter alia, physiological in vitro assays. Such physiological assays may monitor cell death, for example by loss of cell membrane integrity (e.g. FACS based propidium iodide assay, trypan Blue influx assay, photometric enzyme release assays (LDH), radiometric ^{51}Cr release assay, fluorometric Europium release and CalceinAM release assays). Further assays comprise monitoring of cell viability, for example by photometric MTT, XTT, WST-1 and alamarBlue assays, radiometric ^3H -Thd incorporation assay, clonogenic assay measuring cell division activity, and fluorometric Rhodamine 123 assay measuring mitochondrial transmembrane gradient. In addition, apoptosis may be monitored for example by FACS-based phosphatidylserin exposure assay, ELISA-based TUNEL test, caspase activity assay (photometric, fluorometric or ELISA-based) or analysing changed cell morphology (shrinking, membrane blebbing). It is preferred that cytotoxic activity is analysed by FACS-based measurements of release of fluorescence-based dyes. In such an assay fluorescence labelled cells, which carry a molecule which binds to the second domain of the cytotoxically active bispecific CD3 binding construct of the invention (preferably, NALM-6 cells for CD19 and Kato cells for the EpCAM antigen) are incubated with isolated PBMCs of random donors or with a standardized T-cell line in the presence of the cytotoxically active bispecific CD3 binding construct of the invention. After incubation, the release of the dye from the fluorescent target cells into the supernatant is determined by a spectrofluorimeter. A cytotoxically active deimmunized bispecific CD3 binding construct of the present invention is characterized by comparing values obtained by measuring the bioactivity of a similar construct which is not deimmunized or has no specificity to the target cells.

The term "binding to/interacting with" as used in the context with the present invention defines a binding/interaction of at least two "antigen-interaction-sites" with

each other. The term "antigen-interaction-site" defines, in accordance with the present invention, a motif of a polypeptide which shows the capacity of specific interaction with a specific antigen or a specific group of antigens. Said binding/interaction is also understood to define a "specific recognition". The term "specifically recognizing" means in accordance with this invention that the antibody molecule is capable of specifically interacting with and/or binding to at least two amino acids of each of the human target molecule as defined herein. Antibodies can recognize, interact and/or bind to different epitopes on the same target molecule. Said term relates to the specificity of the antibody molecule, i.e. to its ability to discriminate between the specific regions of the human target molecule as defined herein. The specific interaction of the antigen-interaction-site with its specific antigen may result in an initiation of a signal, e.g. due to the induction of a change of the conformation of the antigen, an oligomerization of the antigen, etc. Thus, specific motif in the amino acid sequence of the antigen-interaction-site and the antigen bind to each other as a result of their primary, secondary or tertiary structure as well as the result of secondary modifications of said structure.

The term "specific interaction" as used in accordance with the present invention means that the CD3 specific binding construct of the invention does not or essentially does not cross-react with (poly)peptides of similar structures. Accordingly, the construct of the invention specifically binds to/interacts with human CD3 and is capable, due to its second, Ig-derived domain to interact with specific, selected other compounds, antigens, cell surface markers, tumor markers, etc. Specific examples of such molecules against which said second, Ig-derived domain is directed are given herein below.

Cross-reactivity of a panel of constructs under investigation may be tested, for example, by assessing binding of said panel of bispecific single chain constructs under conventional conditions (see, e.g., Harlow and Lane, Antibodies: A Laboratory Manual, Cold Spring Harbor Laboratory Press, 1988 and Using Antibodies: A Laboratory Manual, Cold Spring Harbor Laboratory Press, 1999) to the (poly)peptide of interest as well as to a number of more or less (structurally and/or functionally) closely related (poly)peptides. Only those constructs (i.e. antibodies, (bispecific) scFvs and the like) that bind to the (poly)peptide/protein of interest but do not or do not essentially bind to any of the other (poly)peptides which are preferably expressed by the same tissue as the (poly)peptide of interest, e.g. by the cells of the heart

tissue, are considered specific for the (poly)peptide/protein of interest and selected for further studies in accordance with the method provided herein and illustrated in the appended examples. These methods may comprise, inter alia, binding studies, blocking and competition studies with structurally and/or functionally closely related molecules. These binding studies also comprise FACS analysis, surface plasmon resonance (SPR, e.g. with BIAcore®), analytical ultracentrifugation, isothermal titration calorimetry, fluorescence anisotropy, fluorescence spectroscopy or by radiolabeled ligand binding assays. Furthermore, physiological assays, like cytotoxic assays (as illustrated in the examples) and assays mentioned above may be performed. Accordingly, examples for the specific interaction of an antigen-interaction-site with a specific antigen may comprise the specificity of a ligand for its receptor. Said definition particularly comprises the interaction of ligands which induce a signal upon binding to its specific receptor. Examples for corresponding ligands comprise cytokines which interact/bind with/to its specific cytokine-receptors. Also particularly comprised by said definition is the binding of an antigen-interaction-site to antigens such as antigens of the selectin family, integrins and of the family of growth factors like EGF. An other example for said interaction, which is also particularly comprised by said definition, is the interaction of an antigenic determinant (epitope) with the antigenic binding site of an antibody.

The term "binding to/interacting with" relates not only to a linear epitope but may also relate to a conformational epitope, a structural epitope or a discontinuous epitope consisting of two regions of the human target molecules or parts thereof. In context of this invention, a conformational epitope is defined by two or more discrete amino acid sequences separated in the primary sequence which come together on the surface of the molecule when the polypeptide folds to the native protein (Sela, (1969) Science 166, 1365 and Laver, (1990) Cell 61, 553-6).

The term "discontinuous epitope" means in context of the invention non-linear epitopes that are assembled from residues from distant portions of the polypeptide chain. These residues come together on the surface when the polypeptide chain folds into a three-dimensional structure to constitute a conformational/structural epitope.

The constructs of the present invention are also envisaged to specifically bind to/interact with a conformational/structural epitope(s) composed of and/or comprising the two regions of the human CD3 complex described herein or parts thereof as

disclosed herein below.

Accordingly, specificity can be determined experimentally by methods known in the art and methods as disclosed and described herein. Such methods comprise, but are not limited to Western blots, ELISA-, RIA-, ECL-, IRMA-tests and peptide scans.

5

The term "Ig-derived second binding domain" relates to an "immunoglobulin-derived domain", specifically to an antibody or fragments thereof, to single chain antibodies, to synthetic antibodies, to antibody fragments, such as Fab, a F(ab₂)', Fv or scFv fragments etc, or a chemically modified derivative of any of these. These antibodies

10 molecules may be derived from different species or may be of chimeric origin. Most preferably (as documented herein below), said Ig-derived second domain comprised in the CD3 specific binding construct of the invention is a scFv. Antibodies, antibody constructs, antibody fragments, antibody derivatives (all being Ig-derived) to be employed in accordance with the invention or their corresponding immunoglobulin

15 chain(s) can be further modified using conventional techniques known in the art, for example, by using amino acid deletion(s), insertion(s), substitution(s), addition(s), and/or recombination(s) and/or any other modification(s) known in the art either alone or in combination. Methods for introducing such modifications in the DNA sequence underlying the amino acid sequence of an immunoglobulin chain are well known to

20 the person skilled in the art; see, e.g., Sambrook (1989), loc. cit. The term "Ig-derived domain" particularly relates to (poly)peptide constructs comprising at least one CDR. Fragments or derivatives of the recited Ig-derived domains define (poly)peptides which are parts of the above antibody molecules and/or which are modified by chemical/biochemical or molecular biological methods. Corresponding methods are

25 known in the art and described inter alia in laboratory manuals (see Sambrook et al.; Molecular Cloning: A Laboratory Manual; Cold Spring Harbor Laboratory Press, 2nd edition 1989 and 3rd edition 2001; Gerhardt et al.; Methods for General and Molecular Bacteriology; ASM Press, 1994; Lefkovits; Immunology Methods Manual: The Comprehensive Sourcebook of Techniques; Academic Press, 1997; Golemis;

30 Protein-Protein Interactions: A Molecular Cloning Manual; Cold Spring Harbor Laboratory Press, 2002).

The term "deimmunized" as used herein relates to the above-identified first domain of the inventive CD3 binding construct, wherein said first domain is modified compared

to an original wild type construct by rendering said wild type construct non-immunogenic or less immunogenic in humans. Wild type constructs according to the invention relate to antibodies or parts thereof (like frameworks and/or CDRs) of non-human origin. Corresponding examples are antibodies or fragments thereof as

5 described in US 4,361,549 or WO 99/54440. The term "deimmunized" also relates to constructs, which show reduced propensity to generate T cell epitopes. In accordance with this invention, the term "reduced propensity to generate T cell epitopes" relates to the removal of T-cell epitopes leading to specific T-cell activation. Furthermore, reduced propensity to generate T cell epitopes means substitution of

10 amino acids contributing to the formation of T cell epitopes, i.e. substitution of amino acids, which are essential for formation of a T cell epitope. In other words, reduced propensity to generate T cell epitopes relates to reduced immunogenicity or reduced capacity to induce antigen independent T cell proliferation. In addition, reduced propensity to generate T cell epitopes relates to deimmunisation, which means loss

15 or reduction of potential T cell epitopes of amino acid sequences inducing antigen independent T cell proliferation. According to the invention, a CD3 binding region, which has reduced propensity to generate T cell epitopes is less or preferably non immunogenic compared to non-deimmunized molecule but which has still retained its capacity to binding to CD3, i.e. a low/non immunogenic antibody construct binding to

20 CD3. The term "T cell epitope" relates to short peptide sequences which can be released during the degradation of peptides, polypeptides or proteins within cells and subsequently be presented by molecules of the major histocompatibility complex (MHC) in order to trigger the activation of T cells; see inter alia WO 02/066514. For peptides presented by MHC class II such activation of T cells can then give rise to an

25 antibody response by direct stimulation of T cells to produce said antibodies. Accordingly, a deimmunized first domain specifically binding to a human CD3 comprises at least the above mentioned CDR-H3 located between framework H3 and H4, wherein said first binding domain shows a reduced propensity to generate T-cell epitopes compared to a non-deimmunized first domain comprising the unchanged wt-

30 CDR-H3 located between framework H3 and H4. Furthermore, said deimmunized first domain comprises at least in the transition region of the framework H1 and CDR-H1 the above mentioned sequence motif which provides a reduced propensity to generate T-cell epitopes compared to a non-deimmunized first domain comprising the unchanged wt-H1 transition region of the framework H1 and CDR-H1.

“Reduced propensity to generate T-cell epitopes” and/or “deimmunization” may be measured by techniques known in the art. Preferably, de-immunization of proteins may be tested in vitro by T cell proliferation assay. In this assay PBMCs from donors representing > 80 % of HLA-DR alleles in the world are screened for proliferation in response to either wild type or de-immunized peptides. Ideally cell proliferation is only detected upon loading of the antigen-presenting cells with wild type peptides. Alternatively, one may test deimmunization by expressing HLA-DR tetramers representing all haplotypes. These tetramers may be tested for peptide binding or loaded with peptides substitute for antigen-presenting cells in proliferation assays. In order to test if de-immunized peptides are presented on HLA-DR haplotypes, binding of e.g. fluorescence-labeled peptides on PBMCs can be measured. Furthermore, de-immunization can be proven by determining whether antibodies against the de-immunized molecules have been formed after administration in patients. A particular preferred method is a T-cell proliferation assay as, inter alia, shown in appended example 6.

Preferably, antibody derived molecules are deimmunized in the framework regions and most of the CDR regions are not modified in order to generate reduced propensity to induce T cell epitope so that the binding affinity of the CDR regions is not affected. Even elimination of one T cell epitope results in reduced immunogenicity. Preferably, the molecule is deimmunized in the CDR2 region of the VL chain, more preferably in the CDR2 region of the VH chain, even more preferably in the CDR1 region of the VL chain, even more preferably in the CDR1 region of the VH chain, more preferably in the framework region (FR) of the VL chain and most preferably in the framework region (FR) of the VH chain.

25

The term “CDR” as employed herein relates to “complementary determining region”, which is well known in the art. The CDRs are parts of immunoglobulins and T cell receptors that determine the specificity of said molecules and make contact with specific ligand. The CDRs are the most variable part of the molecule and contribute to the diversity of these molecules. There are three CDR regions CDR1, CDR2 and CDR3 in each V domain. CDR-H depicts a CDR region of a variable heavy chain and CDR-L relates to a CDR region of a variable light chain. H means the variable heavy chain and L means the variable light chain. The CDR regions of an Ig-derived region may be determined as described in Kabat (1991). Sequences of Proteins of

30

Immunological Interest, 5th edit., NIH Publication no. 91-3242 U.S. Department of Health and Human Services, Chothia (1987). J. Mol. Biol. 196, 901-917 and Chothia (1989) Nature, 342, 877-883.

5 In general CDR-L1 consists of 10-17 amino acid residues, starts approximately at amino acid residue 24 of the full VL region of an Ig-derived sequence and the residue Cys precedes the CDR-L1. Preferably, the residue Trp follows CDR-L1. CDR-L2 starts preferably, 16 amino acid residues after CDR-L1 and consists preferably of 7 residues. Preferably, the amino acid residues Ile-Tyr, but also, Val-Tyr, Ile-Lys, Ile-
 10 Phe precede CDR-L2. CDR-L3 starts, preferably, 33 amino acid residues after CDR-L2 and consists, preferably, of 7-11 residues. CDR-L3 follows, preferably, the residue Cys and, preferably, the residues Phe-Gly-Xaa-Gly follow directly CDR-L3. CDR-H1 consists of, preferably, 10-12 residues and starts, preferably, approximately at residue 26 from the beginning of the VH region. Preferably, the residue Trp follows
 15 CDR-H1. CDR-H2 starts, preferably, 15 amino acid residues after the end of CDR-H1 and consists, preferably, of 16 to 19 residues. Preferably, residues Lys/Arg-Leu/Ile/Val/Phe/Thr/Ala-Thr/Ser/Ile/Ala follow CDR-H2. CDR-H3 starts 33 amino acid residues after CDR-H2 and has a length of 3-25 amino acid residues. CDR-H3 follows the sequence Cys-Xaa-Xaa (preferably Cys-Ala-Arg) and the residues Trp-
 20 Gly-Xaa-Gly follow CDR-H3. The structure of CDR region has been described in <http://www.bioinf.org.uk/abs/>.

● The above recited CDR-H1 and CDR-H2 regions are derived from antibody molecules which are capable of specifically binding to/interacting with human CD3.
 25 Such CD3 specific antibody are known in the art and comprise in particular the monoclonal antibodies OKT-3, TR-66 or X35-3, VIT3, BMA030 (BW264/56), CLB-T3/3, CRIS7, YTH12.5, F111-409, CLB-T3.4.2, TR-66, WT32, SPv-T3b, 11D8, XIII-141, XIII-46, XIII-87, 12F6, T3/RW2-8C8, T3/RW2-4B6, OKT3D, M-T301, SMC2, F101.01, UCHT-1 or WT-31. All the mentioned anti-CD3 antibodies are human
 30 specific and in accordance with this invention it is possible to combine various CDR regions, in particular CDRH regions of the antibodies.

In a more preferred embodiment, said CDR-H1 and CDR-H2 regions of said CD3 specific domain with reduced propensity to generate T cell epitopes are derived from

the antibody construct described in WO 99/54440. Even more preferred (and as illustrated in the appended examples) said CDR-H1 and CDR-H2 regions, as well as the CDR-H3 region, are derived from an antibody/antibody derivative with specificity for the CD3 molecule described by Traunecker (1991), EMBO J. 10, 3655-3659. In accordance with this invention, said CDR-H1, CDR-H2 and CDR-H3 regions are derived from antibodies/antibody derivatives and the like which are capable of specifically recognizing the human CD3- ϵ chain in the context of other TCR subunits, e.g. in mouse cells transgenic for human CD3- ϵ chain. These transgenic mouse cells express human CD3- ϵ chain in a native or near native conformation.

In accordance with this invention, a framework region relates to a region in the V domain (VH or VL domain) of immunoglobulins and T-cell receptors that provides a protein scaffold for the hypervariable complementarity determining regions (CDRs) that make contact with the antigen. In each V domain, there are four framework regions designated FR1, FR2, FR3 and FR4. Framework 1 encompasses the region from the N-terminus of the V domain until the beginning of CDR1, framework 2 relates to the region between CDR1 and CDR2, framework 3 encompasses the region between CDR2 and CDR3 and framework 4 means the region from the end of CDR3 until the C-terminus of the V domain; see, inter alia, Janeway, Immunobiology, Garland Publishing, 2001, 5th ed. Thus, the framework regions encompass all the regions outside the CDR regions in VH or VL domains. Furthermore, the term "transition sequence between a framework and a CDR region" relates to a direct junction between the framework and CDR region. In particular, the term "transition sequence between a framework and a CDR region" means the sequence directly located N- and C-terminally of the CDR regions or amino acids surrounding CDR regions. Accordingly, frameworks may also comprise sequences between different CDR regions. The person skilled in the art is readily in a position to deduce from a given sequence the framework regions, the CDRs as well as the corresponding transition sequences; see Kabat (1991) Sequences of Proteins of Immunological Interest, 5th edit., NIH Publication no. 91-3242 U.S. Department of Health and Human Services, Chothia (1987). J. Mol. Biol. 196, 901-917 and Chothia (1989) Nature, 342, 877-883..

A preferred cytotoxically active CD3 specific binding construct of the invention further

comprises in said first domain a framework H3 comprising the sequence Met-Glu-Leu-Ser (MELS; SEQ ID NO:234). Even more preferred is an inventive construct which comprises in said first domain a framework H3 comprising the sequence Ile-Thr-Thr-Asp-Lys (ITTDK; SEQ ID NO: 235).

5

In accordance with the present invention, the first domain of the inventive construct specifically binding to/interacting with human CD3 and having a reduced propensity to generate T cell epitopes, comprises a CDR-H1, CDR-H2 and CDR-H3 regions as defined herein and, in a preferred embodiment, VH-frameworks (frameworks 1, 2, 3, 10 4) as defined above, in particular as shown in any one of SEQ ID NOs.: 152 or 153, 156 or 157, 160 or 161 and/or 164 or 165. Therefore, the CD3 specific binding construct of the invention comprises a first domain which specifically binds to human CD3 and comprises a framework region 1 as shown in SEQ ID NO. 152 or 153, a framework region 2 as shown in SEQ ID NO. 156 or 157, a framework region 3 as 15 shown in SEQ ID NO. 160 or 161 and/or a framework region 4 as shown in SEQ ID NO. 164 or 165.

In a particularly preferred embodiment of the invention, the cytotoxically active deimmunized CD3 specific binding construct comprises in its first domain (a) a CDR- 20 H1 as depicted in SEQ ID NO 88; and (b) a CDR-H2 as depicted in SEQ ID NO 90 or 92.

Accordingly, the modified CDR-H1 and CDR-H2 regions lead to a reduced propensity to generate T cell epitopes and are derived from an CD3- ϵ chain specific antibody. 25 Most preferably in accordance with this invention said (parental) antibodies should be capable of specifically binding epitopes reflecting the native or near native structure or a conformational epitope of human CD3 presented in context of the TCR complex.

Preferably, the CD3 specific binding construct of the invention comprises a VH-region 30 as depicted in SEQ ID NO.74 or 76. SEQ ID NO:74 shows an illustrative deimmunized variable heavy region and, similarly, SEQ ID NO:76 shows an illustrative deimmunized variable heavy region.

Preferably, the inventive CD3 specific binding construct comprises a CDR-L1 as depicted in SEQ ID NO. 98 or 100, a CDR-L2 as depicted in SEQ ID NO.102 and/or a CDR-L3 as depicted in SEQ ID NO.104.

5 The CD3 specific binding construct of the invention comprises, in a preferred embodiment, a VL region in its CD3-specific portion, wherein said VL region is selected from the group consisting of SEQ ID NO 78 , SEQ ID NO 80, SEQ ID NO 82 and SEQ ID NO 112. VL1 as characterized in SEQ ID NO.:78, VL2 as characterized in SEQ ID NO.:80 and VL 3 as characterized in SEQ ID NO.:82 relate to full
10 deimmunized VL regions in accordance with this invention, and they may be used in various combinations with the above described VH regions. Yet, it is also envisaged that the non-deimmunized VL region may be combined, in accordance with the invention, with deimmunized VH regions defined above. A corresponding non-deimmunized VL-region preferably employed in an cytotoxically active CD3 binding
15 construct of the invention, is shown in SEQ ID NO.: 112. Accordingly, not only heavy chain part of the above recited "first domain" of the inventive CD3 construct may be modified to have a reduced propensity to generate T cell epitopes. It is also envisaged that said domain comprises the corresponding variable light chain parts. SEQ ID NOs. 78, 80, and 82, for example, depict deimmunized VL1, VL2 and VL3
20 regions of the CD3 binding part of a construct disclosed in WO 99/54440.

As mentioned above, the CD3 specific binding construct of the invention, most preferably, comprises an Ig-derived second domain which is a scFv. Accordingly, in a most preferred embodiment of the present invention, a deimmunized, bispecific
25 single chain antibody construct is provided with one specificity for human CD3 and a further specificity which is mediated by a second scFv, directed against/capable of interacting with a further molecule/compound. These further molecules/compounds may comprise cell surface molecules, tumor markers, tumor antigens and the like. Such further compounds/molecules are exemplified herein below and specific
30 constructs are also given and provided in the appended examples.

The term "bispecific single chain antibody construct" relates to a construct comprising two antibody derived binding domains, preferably scFvs. One of said binding domains consists of variable regions (or parts thereof) of an antibody, antibody

fragment or derivate thereof, capable of specifically binding to/interacting with human CD 3 antigen (target molecule 1). The second binding domain consists of variable regions (or parts thereof) of an antibody, antibody fragment or derivative thereof, capable of specifically binding to/interacting with another (human) antigen (target molecule 2) as defined below. Accordingly, said second binding domain is, in accordance with this invention, the Ig-derived second domain recited above which comprises an antigen-interaction-site with specificity for a cell surface molecule and/or a tumor specific marker. Said two domains/regions in the bispecific construct, preferably said bispecific single chain antibody construct, are preferably covalently connected to one another as a single chain. This connection can be effected either directly (domain 1 [specific for human CD3 antigen, comprising a reduced propensity to generate T cell epitopes and comprising CDR-regions or CDR-regions and framework regions as defined above] – domain 2 [specific for a cell surface molecule and/or a tumor specific marker] or domain 1 [specific for a cell surface molecule and/or a tumor specific marker] – domain 2 [specific for human CD3 antigen, comprising a reduced propensity to generate T cell epitopes and comprising CDR-regions or CDR-regions and framework regions as defined above]) or through an additional polypeptide linker sequence (domain1 – linker sequence – domain2). In the event that a linker is used, this linker is preferably of a length and sequence sufficient to ensure that each of the first and second domains can, independently from one another, retain their differential binding specificities. As mentioned above and as documented in the appended examples, preferably, the CD3 specific binding construct comprising at least two domains as defined herein is a “bispecific single chain antibody construct”, most preferably a bispecific single chain Fv (scFv). It is in particular envisaged that said construct is employed in context of a pharmaceutical composition. Bispecific single chain molecules are known in the art and are described in WO 99/54440, Mack, J. Immunol. (1997), 158, 3965-3970, Mack, PNAS, (1995), 92, 7021-7025, Kufer, Cancer Immunol. Immunother., (1997), 45, 193-197, Löffler, Blood, (2000), 95, 6, 2098-2103, Brühl, J. Immunol., (2001), 166, 2420-2426. A particularly preferred molecular format of the invention provides a polypeptide construct wherein the CD3 specific binding domain of the construct of the invention comprises at least one V_H and one V_L region as defined above. It is of note that in addition to a V_H -region as defined herein and having reduced propensity to generate T cell epitopes, said specific binding construct may comprise additional

regions/domains with reduced propensity to generate T cell epitopes. As mentioned above, also the VL-region and/or the corresponding frameworks may comprise amino acid stretches which have been engineered in accordance with this invention to having reduced propensity for T cell epitope generation. The intramolecular orientation of the V_H-domain and the V_L-domain, which are linked to each other by a linker-domain, in the scFv format is not decisive for the recited bispecific single chain constructs. Thus, scFvs with both possible arrangements (V_H-domain – linker domain – V_L-domain; V_L-domain – linker domain – V_H-domain) are particular embodiments of the recited bispecific single chain construct. A CD3 specific domain can be located N- or C-terminally in the bispecific molecule. V_H and V_L regions of each domain can be arranged in different orders (V_H-V_L or V_L-V_H).

The term "single-chain" as used in accordance with the present invention means that said first and second domain of the bispecific single chain construct are covalently linked, preferably in the form of a co-linear amino acid sequence encoded by a single nucleic acid molecule.

It is of note that the construct of the invention may comprise, in addition to the herein defined first domain and the Ig-derived second domain (an) additional domain(s), e.g. for the isolation and/or preparation of recombinantly produced constructs.

It is of note that, in accordance with this invention, not only the above described first domain which specifically binds to human CD3 of the inventive CD3 construct may have reduced propensity to generate T cell epitopes. It is also envisaged that the Ig-derived second domain and/or (a) connecting linker-region(s) is (are) modified, for example humanized and/or also deimmunized.

As mentioned above, deimmunization approaches are in particular illustrated in WO 92/10755, WO 00/34317, WO 98/52976, WO 02/079415 or WO 02/012899 and the appended examples. These approaches entail carrying out substitutions of amino acids within potential T cell epitopes. In this way, the likelihood that a given sequence will give rise to T cell epitopes upon intracellular protein processing is reduced.

Furthermore, "humanization approaches" are well known in the art and in particular described for antibody molecules, e.g. Ig-derived molecules. The term "humanized" refers to humanized forms of non-human (e.g., murine) antibodies or fragments thereof (such as Fv, Fab, Fab', F(ab')), scFvs, or other antigen-binding partial sequences of antibodies) which contain some portion of the sequence derived from non-human antibody. Humanized antibodies include human immunoglobulins in which residues from a complementary determining region (CDR) of the human immunoglobulin are replaced by residues from a CDR of a non-human species such as mouse, rat or rabbit having the desired binding specificity, affinity and capacity. In general, the humanized antibody will comprise substantially all of at least one, and generally two, variable domains, in which all or substantially all of the CDR regions correspond to those of a non-human immunoglobulin and all or substantially all of the FR regions are those of a human immunoglobulin consensus sequence. The humanized antibody optimally also will comprise at least a portion of an immunoglobulin constant region (Fc), typically that of a human immunoglobulin; see, inter alia, Jones et al., *Nature* 321:522-525 (1986), Presta, *Curr. Op. Struct. Biol.* 2:593-596 (1992). Methods for humanizing non-human antibodies are well known in the art. Generally, a humanized antibody has one or more amino acids introduced into it from a source which is non-human in order to more closely resemble a human antibody, while still retaining the original binding activity of the antibody. Methods for humanization of antibodies/antibody molecules are further detailed in Jones et al., *Nature* 321:522-525 (1986); Riechmann et al., *Nature* 332:323-327 (1988); and Verhoeyen et al., *Science* 239:1534-1536 (1988). Specific examples of humanized antibodies, e.g. antibodies directed against EpCAM, are known in the art, see e.g. (LoBuglio, Proceedings of the American Society of Clinical Oncology (Abstract), 1997, 1562 and Khor, Proceedings of the American Society of Clinical Oncology (Abstract), 1997, 847).

Accordingly, in the context of this invention, in particular bispecific single chain antibody constructs are provided, which are deimmunized and can successfully be employed in pharmaceutical compositions.

As mentioned above, the Ig-derived second domain of the above-described CD3 specific binding construct may comprise an antigen-interaction-site with specificity for

a cell surface molecule.

The term "cell surface molecule", as used herein, also denotes molecules which are presented on the surface of cells. The term "cell surface molecule", relates to molecules, which are presented on the surface of cells and comprise domains or epitopes accessible (in vitro or in vivo) to Ig-derived binding domains, preferably antibodies, antibody fragments or derivatives. As illustrated above, most preferably said Ig-derived domain is a scFv. Examples for said cell surface molecules are membrane and transmembrane proteins, molecules adapted to said proteins or the cell surface etc. According to a further preferred embodiment of the invention said cell surface molecule is a tumor specific marker. In context of this invention, the term "tumor specific marker" relate to molecules, which are presented and/or located on the surface of tumor cells or which are ubiquitously expressed but are only accessible for binding of antibodies, antibody fragments or antibody derivatives on the surface of tumor cells. Examples of tumor markers are given herein below and comprise, but are not limited to, EpCAM, CD19, HER-2, HER-2 neu, HER-3, HER-4, EGFR, PSMA, CEA, MUC-1 (mucin), MUC2, MUC3, MUC4, MUC5_{AC}, MUC5_B, MUC7, Lewis-Y, CD20, CD33, CD30, CD44v6, Wue-1, Plasma Cell Antigen (see WO 01/47953), (membrane-bound) IgE, Melanoma Chondroitin Sulfate Proteoglycan (MCSP), STEAP, mesothelin, Prostate Stem Cell Antigen (PSCA), sTn (sialylated Tn antigen), FAP (fibroblast activation antigen), EGFRvIII, Ig α , Ig β , MT-MMPs, Cora antigen, EphA2, L6 and CO-29.

The Ig-derived second domain of the CD3 specific binding construct of the invention may also comprise an antigen-interaction site with a specificity for a molecule selected from the group consisting of EpCAM, CCR5, CD19, HER-2, HER-2 neu, HER-3, HER-4, EGFR, PSMA, CEA, MUC-1 (mucin), MUC2, MUC3, MUC4, MUC5_{AC}, MUC5_B, MUC7, β hCG, Lewis-Y, CD20, CD33, CD30, ganglioside GD3, 9-O-Acetyl-GD3, GM2, Globo H, fucosyl GM1, Poly SA, GD2, Carboanhydrase IX (MN/CA IX), CD44v6, Sonic Hedgehog (Shh), Wue-1, Plasma Cell Antigen, (membrane-bound) IgE, Melanoma Chondroitin Sulfate Proteoglycan (MCSP), CCR8, TNF-alpha precursor, STEAP, mesothelin, A33 Antigen, Prostate Stem Cell Antigen (PSCA), Ly-6; desmoglein 4, E-cadherin neoepitope, Fetal Acetylcholine Receptor, CD25, CA19-9 marker, CA-125 marker and Muellarian Inhibitory Substance (MIS) Receptor type II, sTn (sialylated Tn antigen), FAP (fibroblast

activation antigen), endosialin, EGFRvIII, L6, SAS, CD63, TAG72, TF-antigen, Cora antigen, CD7, CD22, Ig α (CD79a), Ig β (CD79b), G250, gp100, MT-MMPs, F19-antigen, CO-29 and EphA2.

- 5 The constructs provided herein are particularly useful in medical setting. For example, tumorous diseases and/or lymphomas, preferably non-Hodgkin's B-cell lymphoma, may be treated with an inventive deimmunized (bispecific) construct directed against human CD3 and CD20 (CD3xCD20 or CD20xCD3). Autoimmune diseases may be treated by the administration of deimmunized (bispecific) constructs directed against
- 10 human CD3 and CD30 or CD19 (i.e. CD3xCD30 or CD30xCD3 or CD3xCD19 or CD19xCD3). Rheumatoid arthritis, as well as other inflammatory diseases may be treated with an inventive deimmunized (bispecific) construct directed against human CD3 and CCR5 (CD3xCCR5 or CCR5xCD3). A deimmunized CD3 specific binding construct as defined herein and comprising a second Ig-derived domain directed
- 15 to/binding with TNF-alpha precursor may also be useful in the treatment or prevention of inflammatory disorders. CD3 constructs as provided herein and comprising a second, Ig-derived domain directed against/binding to/interacting with EpCAM, CD19, HER-2, HER-2 neu, HER-3, HER-4, EGFR, PSMA, CEA, MUC-1 (mucin), MUC2, MUC3, MUC4, MUC5_{AC}, MUC5_B, MUC7, Lewis-Y, CD20, CD33,
- 20 CD30, CD44v6, Wue-1, Plasma Cell Antigen (see WO 01/47953), (membrane-bound) IgE, Melanoma Chondroitin Sulfate Proteoglycan (MCSP), STEAP, mesothelin, Prostate Stem Cell Antigen (PSCA), sTn (sialylated Tn antigen), FAP (fibroblast activation antigen), EGFRvIII, Ig α , Ig β , MT-MMPs, Cora antigen, EphA2, L6 and CO-29 may be particularly useful in the medical intervention of tumorous
- 25 diseases like breast cancer, colon cancer, prostate cancer, head and neck cancer, skin cancer (melanoma), cancers of the genito-urinary tract, e.g. ovarian cancer, endometrial cancer, cervix cancer and kidney cancer, lung cancer, gastric cancer, cancer of the small intestine, liver cancer, pancreas cancer, gall bladder cancer, cancers of the bile duct, esophagus cancer, cancer of the salivary glands and
- 30 cancer of the thyroid gland or other tumorous diseases like hematological tumors, gliomas, sarcomas or osteosarcomas. The administration of the CD3 binding constructs is also indicated for minimal residual disease, preferably for early solid tumors, advanced solid tumors or metastatic solid tumors.

As also illustrated in the appended examples, a particularly preferred CD3 specific binding construct of the invention comprises the above defined first domain with reduced propensity to generate T cell epitopes and a second, Ig-derived domain comprising an antigen-interaction site with a specificity for EpCAM.

5

Epithelial cell adhesion molecule (EpCAM, also called 17-1A antigen, KSA, EGP40, GA733-2, ks1-4 or esa) is a 40-kDa membrane-integrated glycoprotein of 314 amino acids with specific expression in certain epithelia and on many human carcinomas (reviewed in Balzar, J. Mol. Med. 1999, 77, 699-712). EpCAM was discovered and subsequently cloned through its recognition by the murine monoclonal antibody 17-1A/edrecolomab (Goettlinger, Int J Cancer. 1986; 38, 47-53 and Simon, Proc. Natl. Acad. Sci. USA. 1990; 87, 2755-2759). EpCAM serves to adhere epithelial cells in an oriented and highly ordered fashion (Litvinov, J Cell Biol. 1997, 139, 1337-1348). Upon malignant transformation of epithelial cells the rapidly growing tumor cells are abandoning the high cellular order of epithelia. Consequently, the surface distribution of EpCAM becomes less restricted and the molecule better exposed on tumor cells and accessible for binding of antibodies, antibody fragments or antibody derivatives on the surface of tumor cells. Due to their epithelial cell origin, tumor cells from most carcinomas still express EpCAM on their surface.

20

In vivo, expression of EpCAM is related to increased epithelial proliferation and negatively correlates with cell differentiation (for review see Balzar, 1999, J. Mol. Med. 77, 699-712). Expression of EpCAM is essentially seen with all major carcinomas (reviewed in Balzar, J Mol Med. 1999, 77, 699-712 or documented, inter alia, in De Bree, Nucl Med Commun. 1994, 15, 613-27; Zhang, Clin Cancer Res. 1998, 4, 295-302). Because of its widespread expression, EpCAM is referred to as a "pan-carcinoma" antigen. In many cases, tumor cells were observed to express EpCAM to a much higher degree than their parental epithelium or less aggressive forms of said cancers. For example, increased EpCAM expression represents an early event in the development of prostate cancer (Poczatek, J Urol., 1999, 162, 1462-1644). In addition, in the majority of both squamous and adenocarcinomas of the cervix a strong EpCAM expression correlates with an increased proliferation and the disappearance of markers for terminal differentiation (Litvinov, Am. J. Pathol. 1996, 148, 865-75). In breast cancer, overexpression of EpCAM on tumor cells is a

30

predictor of survival (Gastl, Lancet. 2000, 356, 1981-1982). EpCAM is a marker for the detection of disseminated tumor cells in patients suffering from squamous cell carcinoma of the head, neck and lung (Chaubal, Anticancer Res 1999, 19, 2237-2242, Piyathilake, Hum Pathol. 2000, 31, 482-487). Normal squamous epithelium, as found in epidermis, oral cavity, epiglottis, pharynx, larynx and esophagus did not significantly express EpCAM (Quak, Hybridoma, 1990, 9, 377-387). EpCAM has been shown to be expressed on the majority of primary, metastatic, and disseminated NSCLC (non small cell lung cancer cells (Passlick, Int J Cancer, 2000, 87, 548-552)), on gastric and gastro-oesophageal junction adenocarcinomas (Martin, J Clin Pathol 1999, 52, 701-4) and in cell lines derived from colorectal, pancreatic carcinomas and breast carcinomas (Szala, Proc Natl Acad Sci U S A 1990, 87, 3542-6, Packeisen, Hybridoma, 1999, 18, 37-40).

In a most preferred embodiment, the CD3 specific binding construct of the invention which comprises a second Ig-derived domain directed against/binding to EpCAM, comprises an amino acid sequence selected from the group of

- (a) an amino acid sequence as shown in any one of SEQ ID NO 31, 33, 35, 37, 39, 49, 55, 58, 61, 63, 65, 67, 237, 239, 241, 243, 245, 247, 249, 251, 253, 255, 257, 259, 261, 263, 265, 267, 269, 271, 273, 275, 277, 279, 281, 283, 285, 287, 289, 291, 293, 295, 297, 299, 301, 303, 305, 307, 309, 311, 313, 315, 317, 319, 321, 323 and 325;
- (b) an amino acid sequence encoded by a nucleic acid sequence as shown in any one of SEQ ID NO 30, 32, 34, 36, 38, 48, 54, 57, 60, 62, 64, 66, 236, 238, 240, 242, 244, 246, 248, 250, 252, 254, 256, 258, 260, 262, 264, 266, 268, 270, 272, 274, 276, 278, 280, 282, 284, 286, 288, 290, 292, 294, 296, 298, 300, 302, 304, 306, 308, 310, 312, 314, 316, 318, 320, 322 and 324; and
- (c) an amino acid sequence encoded by a nucleic acid sequence which is degenerate as a result of the genetic code to a nucleotide sequence of (b).

Accordingly, the present invention provides, in a particularly preferred embodiment for specific CD3 constructs which comprise a CD3 binding/interaction part ("anti-CD3") which has reduced propensity to generate T cell epitopes and a further single chain part (an Ig-derived domain) which specifically interacts with/binds to EpCAM ("anti-EpCAM"). The following tables 1A, 1B, 2A, 2B, 3A, 3B, 4A, 4B, 5A and 5B relate to preferred configurations of such CD3 and EpCAM binding constructs.

EpCAM 3-1, EpCAM 3-5, EpCAM 4-1, EpCAM 4-7 and EpCAM 5-10 relate to specific single chain antibodies against EpCAM isolated by phage display in WO99/25818.

Each protein construct in Tables 1A, 2A, 3A, 4A and 5A comprises 7 distinct protein modules, denoted A-G. Protein modules A-G are directly and covalently linked to one another in a single contiguous polypeptide chain by peptide bonds in the order A-B-C-D-E-F-G, with protein module A at the N-terminus and protein module G at the C-terminus. Protein modules A, C, E and G denote antibody variable domains which can be either VH or VL domains of antibodies having specificity for the human CD3 or EpCAM antigen. The modules B, D and F are linkers connecting the VH and VL domains.

If protein module A is a VH antibody domain, then protein module C is a VL protein domain, and vice versa. If protein module E is a VH antibody domain, then protein module G is a VL protein domain, and vice versa.

Deimmunized VH domains of antibodies having specificity for the human CD3 antigen can be selected from the sequences as set out in SEQ ID NOs: 74 or 76. Deimmunized VL domains of antibodies having specificity for the human CD3 antigen can be selected from the sequences as set out in SEQ ID NOs: 78, 80 or 82. The VH protein domain of human EpCAM 3-1, 3-5, 4-1, 4-7 and 5-10 antibody is as set out in SEQ ID NO: 137, 141, 145, 149 and 133, respectively. The VL protein domain of human EpCAM 3-1, 3-5, 4-1, 4-7 and 5-10 antibody is as set out in SEQ ID NO: 139, 143, 147, 151 and 135, respectively.

Pairs of antibody variable domains denoted by the protein module pairs A/C and E/G are joined by additional linking protein modules, wherein protein module B serves to directly link the module pair A/C and protein module F serves to directly link the module pair E/G. When either the module pair A/C or E/G is a pair of deimmunized VH/VL or VL/VH protein domains from an antibody having specificity for the human CD3 antigen, protein module B or F, respectively, has the amino acid sequence as set out in SEQ ID NO: 3. When either the module pair A/C or E/G is a pair of VH/VL or VL/VH from an antibody having specificity for the EpCAM antigen, protein module B or F, respectively, has the amino acid sequence as set out in SEQ ID NO: 168. The module D connects the ABC and EFG module groups.

The combination of protein modules A-B-C and the combination of protein modules E-F-G each respectively constitute one scFv fragment of an antibody having

specificity for either the human CD3 antigen or for the EpCAM antigen. If the modules A and C show the CD3 binding sequence, the respective groups of protein modules A-B-C and E-F-G are connected to each other through protein module D, having the sequence as set out in SEQ ID NO: 176. On the other hand, if the modules A and C show the EpCAM binding sequence, the respective groups of protein modules A-B-C and E-F-G are connected to each other through protein module D, having the sequence as set out in SEQ ID NO: 174. Thus, an additional serine may be inserted after the VL chain for cloning purposes. However, the skilled artisan may also use the linker as shown in SEQ ID NO.:174 in order to link a VL domain with the subsequent V domain instead of SEQ ID NO.:176. Protein module D serves to connect the C-terminal end of protein module C with the N-terminal end of protein module E.

Each nucleic acid construct in Tables 1B, 2B, 3B, 4B and 5B comprises 7 distinct nucleic acid modules, denoted A-G. Nucleic acid modules A-G are directly and covalently linked to one another in a single contiguous nucleotide chain by phosphate glycoside bonds in the order A-B-C-D-E-F-G, with nucleic acid module A at the 5'-end and nucleic acid module G at the 3'-end of a respective nucleic acid construct. Nucleic acid modules A, C, E and G denote encoding regions for antibody variable domains which can be either VH or VL domains of antibodies having specificity for the human CD3 or EpCAM antigen.

If nucleic acid module A encodes a VH antibody domain, then nucleic acid module C encodes a VL protein domain, and vice versa. If nucleic acid module E encodes a VH antibody domain, then nucleic acid module G encodes a VL protein domain, and vice versa.

Nucleic acid molecules encoding deimmunized VH domains of antibodies having specificity for the human CD3 antigen can be selected from the sequences as set out in SEQ ID NOs: 73 or 75. Nucleic acid molecules encoding deimmunized VL domains of antibodies having specificity for the human CD3 antigen can be selected from the sequences as set out in SEQ ID NOs: 77, 79 or 81. The nucleic acid molecule encoding the VH protein domain of the human EpCAM 3-1, 3-5, 4-1, 4-7 and 5-10 antibody is as set out in SEQ ID NO: 136,140, 144, 148 and 132

respectively. The nucleic acid molecule encoding the VL protein domain of the human EpCAM 3-1, 3-5, 4-1, 4-7 and 5-10 antibody is as set out in SEQ ID NO: 138, 142, 146, 150 and 134, respectively.

- 5 Pairs of nucleic acids encoding antibody variable domains denoted by the nucleic acid module pairs A/C and E/G are joined by additional linking nucleic acid modules, wherein nucleic acid module B serves to directly link the module pair A/C and nucleic acid module F serves to directly link the module pair E/G. When either the module pair A/C or E/G denotes nucleic acid encoding a pair of deimmunized VH/VL or
- 10 VL/VH protein domains from an antibody having specificity for the human CD3 antigen, nucleic acid module B or F, respectively, has the nucleotide sequence as set out in SEQ ID NO: 202. When either the module pair A/C or E/G denotes nucleic acid encoding a pair of VH/VL or VL/VH from an antibody having specificity for the human EpCAM antigen, nucleic acid module B or F, respectively, has the nucleotide
- 15 sequence as set out in SEQ ID NO: 201.

- The combination of nucleic acid modules A-B-C and the combination of nucleic acid modules E-F-G each respectively constitute one scFv fragment of an antibody having specificity for either the human CD3 antigen or for the EpCAM antigen. If the A and C
- 20 modules comprise CD3 binding sequences, the respective groups of nucleic acid modules A-B-C and E-F-G are connected to each other through nucleic acid module D, having the nucleotide sequence as set out in SEQ ID NO: 175. If the A and C modules comprise EpCAM binding sequences, the respective groups of nucleic acid modules A-B-C and E-F-G are connected to each other through nucleic acid module
- 25 D, having the nucleotide sequence as set out in SEQ ID NO: 173. However, as mentioned above, the additional codon encoding a serine (in SEQ ID NO.:175) may be inserted for cloning purposes. The skilled person may link the nucleotide sequence encoding the VL chain directly with the subsequent V domain with the linker as depicted in SEQ ID NO.:173 without the additional codon encoding serine at
- 30 the 5' end of the linker. Nucleic acid module D serves to connect the 3'-end of nucleic acid module C with the 5'-end of nucleic acid module E.

Table 1A

Deimmunized anti-human CD3 constructs comprising single chain anti-EpCAM 3-1 variable regions: amino acid sequence

Construct	SEQ ID NO in construct portion ...							deimmunized anti-CD3 construct / Specificity (N -> C)	Domain Arrangement
	A	B	C	D	E	F	G		
1	80	3	74	176	137	168	139	CD3 (VL2/ VH5)xEPCAM(3-1)	LHHL
2	74	3	80	176	137	168	139	CD3 (VH5/VL2)xEPCAM(3-1)	HLHL
3	80	3	74	176	139	168	137	CD3 (VL2/ VH5)xEPCAM(3-1)	LHLH
4	74	3	80	176	139	168	137	CD3 (VH5/VL2)xEPCAM(3-1)	HLLH
5	139	168	137	174	74	3	80	EPCAM(3-1)xCD3 (VH5/VL2)	LHHL
6	137	168	139	174	74	3	80	EPCAM(3-1)xCD3(VH5/VL2)	HLHL
7	139	168	137	174	80	3	74	EPCAM(3-1)xCD3 (VL2/ VH5)	LHLH
8	137	168	139	174	80	3	74	EPCAM(3-1)xCD3(VL2/ VH5)	HLLH
9	80	3	76	176	137	168	139	CD3 (VL2/ VH7)xEPCAM(3-1)	LHHL
10	76	3	80	176	137	168	139	CD3 (VH7/VL2)xEPCAM(3-1)	HLHL
11	80	3	76	176	139	168	137	CD3 (VL2/VH7)xEPCAM(3-1)	LHLH
12	76	3	80	176	139	168	137	CD3 (VH7/VL2)xEPCAM(3-1)	HLLH
13	139	168	137	174	76	3	80	EPCAM(3-1)xCD3 (VH7/VL2)	LHHL
14	137	168	139	174	76	3	80	EPCAM(3-1)xCD3(VH7/VL2)	HLHL
15	139	168	137	174	80	3	76	EPCAM(3-1)xCD3 (VL2/ VH7)	LHLH
16	137	168	139	174	80	3	76	EPCAM(3-1)xCD3(VL2/ VH7)	HLLH

Table 1B

Deimmunized anti-human CD3 constructs comprising single chain anti-EpCAM 3-1 variable regions: nucleotide sequence

Construct	SEQ ID NO in construct portion ...							deimmunized anti-CD3 construct / Specificity (N -> C)	Domain Arrangement
	A	B	C	D	E	F	G		
1	79	202	73	175	136	201	138	CD3 (VL2/ VH5)xEPCAM(3-1)	LHHL
2	73	202	79	175	136	201	138	CD3 (VH5/VL2)xEPCAM(3-1)	HLHL
3	79	202	73	175	138	201	136	CD3 (VL2/ VH5)xEPCAM(3-1)	LHLH
4	73	202	79	175	138	201	136	CD3 (VH5/VL2)xEPCAM(3-1)	HLLH
5	138	201	136	173	73	202	79	EPCAM(3-1)xCD3 (VH5/VL2)	LHHL
6	136	201	138	173	73	202	79	EPCAM(3-1)xCD3(VH5/VL2)	HLHL
7	138	201	136	173	79	202	73	EPCAM(3-1)xCD3 (VL2/ VH5)	LHLH
8	136	201	138	173	79	202	73	EPCAM(3-1)xCD3(VL2/ VH5)	HLLH
9	79	202	75	175	136	201	138	CD3 (VL2/ VH7)xEPCAM(3-1)	LHHL
10	75	202	79	175	136	201	138	CD3 (VH7/VL2)xEPCAM(3-1)	HLHL
11	79	202	75	175	138	201	136	CD3 (VL2/ VH7)xEPCAM(3-1)	LHLH
12	75	202	79	175	138	201	136	CD3 (VH7/VL2)xEPCAM(3-1)	HLLH
13	138	201	136	173	75	202	79	EPCAM(3-1)xCD3 (VH7/VL2)	LHHL
14	136	201	138	173	75	202	79	EPCAM(3-1)xCD3(VH7/VL2)	HLHL
15	138	201	136	173	79	202	75	EPCAM(3-1)xCD3 (VL2/ VH7)	LHLH
16	136	201	138	173	79	202	75	EPCAM(3-1)xCD3(VL2/ VH7)	HLLH

Table 2A

Deimmunized anti-human CD3 constructs comprising single chain anti-EpCAM 3-5 variable regions: amino acid sequence

Construct	SEQ ID NO in construct portion ...							deimmunized anti-CD3 construct / Specificity (N -> C)	Domain Arrangement
	A	B	C	D	E	F	G		
1	80	3	74	176	141	168	143	CD3 (VL2/VH5)xEPCAM(3-5)	LHHL
2	74	3	80	176	141	168	143	CD3 (VH5/VL2)xEPCAM(3-5)	HLHL
3	80	3	74	176	143	168	141	CD3 (VL2/VH5)xEPCAM(3-5)	LHLH
4	74	3	80	176	143	168	141	CD3 (VH5/VL2)xEPCAM(3-5)	HLLH
5	143	168	141	174	74	3	80	EPCAM(3-5)xCD3 (VH5/VL2)	LHHL
6	141	168	143	174	74	3	80	EPCAM(3-5)xCD3 (VH5/VL2)	HLHL
7	143	168	141	174	80	3	74	EPCAM(3-5)xCD3 (VL2/VH5)	LHLH
8	141	168	143	174	80	3	74	EPCAM(3-5)xCD3 (VL2/ VH5)	HLLH
9	80	3	76	176	141	168	143	CD3 (VL2/VH7)xEPCAM(35)	LHHL
10	76	3	80	176	141	168	143	CD3 (VH7/VL2)xEPCAM(3-5)	HLHL
11	80	3	76	176	143	168	141	CD3 (VL2/VH7)xEPCAM(3-5)	LHLH
12	76	3	80	176	143	168	141	CD3 (VH7/VL2)xEPCAM(3-5)	HLLH
13	143	168	141	174	76	3	80	EPCAM(3-5)xCD3 (VH7/VL2)	LHHL
14	141	168	143	174	76	3	80	EPCAM(3-5)xCD3 (VH7/VL2)	HLHL
15	143	168	141	174	80	3	76	EPCAM(3-5)xCD3 (VL2/VH7)	LHLH
16	141	168	143	174	80	3	76	EPCAM(3-5)xCD3 (VL2/ VH7)	HLLH

Table 2B

Deimmunized anti-human CD3 constructs comprising single chain anti-EpCAM 3-5 variable regions: nucleotide sequence

Construct	SEQ ID NO in construct portion ...							deimmunized anti-CD3 construct / Specificity (N -> C)	Domain Arrangement
	A	B	C	D	E	F	G		
1	79	202	73	175	140	201	142	CD3 (VL2/ VH5)xEPcAM(3-5)	LHHL
2	73	202	79	175	140	201	142	CD3 (VH5/VL2)xEPcAM(3-5)	HLHL
3	79	202	73	175	142	201	140	CD3 (VL2/ VH5)xEPcAM(3-5)	LHLH
4	73	202	79	175	142	201	140	CD3 (VH5/VL2)xEPcAM(3-5)	HLLH
5	142	201	140	173	73	202	79	EPcAM(3-5)xCD3(VH5/VL2)	LHHL
6	140	201	142	173	73	202	79	EPcAM(3-5)xCD3(VH5/VL2)	HLHL
7	142	201	140	173	79	202	73	EPcAM(3-5)xCD3 (VL2/VH5)	LHLH
8	140	201	142	173	79	202	73	EPcAM(3-5)xCD3(VL2/VH5)	HLLH
9	79	202	75	175	140	201	142	CD3 (VL2/ VH7)xEPcAM(3-5)	LHHL
10	75	202	79	175	140	201	142	CD3 (VH7/VL2)xEPcAM(3-5)	HLHL
11	79	202	75	175	142	201	140	CD3 (VL2/ VH7)xEPcAM(3-5)	LHLH
12	75	202	79	175	142	201	140	CD3 (VH7/VL2)xEPcAM(3-5)	HLLH
13	142	201	140	173	75	202	79	EPcAM(3-5)xCD3 (VH7/VL2)	LHHL
14	140	201	142	173	75	202	79	EPcAM(3-5)xCD3(VH7/VL2)	HLHL
15	142	201	140	173	79	202	75	EPcAM(3-5)xCD3 (VL2/VH7)	LHLH
16	140	201	142	173	79	202	75	EPcAM(3-5)xCD3(VL2/VH7)	HLLH

Table 3A

Deimmunized anti-human CD3 constructs comprising single chain anti-EpCAM 4-1 variable regions: amino acid sequence

Construct	SEQ ID NO in construct portion ...							deimmunized anti-CD3 construct / Specificity (N -> C)	Domain Arrangement
	A	B	C	D	E	F	G		
1	80	3	74	176	145	168	147	CD3 (VL2/ VH5)xEPCAM(4-1)	LHHL
2	74	3	80	176	145	168	147	CD3 (VH5/VL2)xEPCAM(4-1)	HLHL
3	80	3	74	176	147	168	145	CD3 (VL2/ VH5)xEPCAM(4-1)	LHLH
4	74	3	80	176	147	168	145	CD3 (VH5/VL2)xEPCAM(4-1)	HLLH
5	147	168	145	174	74	3	80	EPCAM(4-1)xCD3 (VH5/VL2)	LHHL
6	145	168	147	174	74	3	80	EPCAM(4-1)xCD3(VH5/VL2)	HLHL
7	147	168	145	174	80	3	74	EPCAM(4-1)xCD3 (VL2/ VH5)	LHLH
8	145	168	147	174	80	3	74	EPCAM(4-1)xCD3(VL2/ VH5)	HLLH
9	80	3	76	176	145	168	147	CD3 (VL2/ VH7)xEPCAM(4-1)	LHHL
10	76	3	80	176	145	168	147	CD3 (VH7/VL2)xEPCAM(4-1)	HLHL
11	80	3	76	176	147	168	145	CD3 (VL2/ VH7)xEPCAM(4-1)	LHLH
12	76	3	80	176	147	168	145	CD3 (VH7/VL2)xEPCAM(4-1)	HLLH
13	147	168	145	174	76	3	80	EPCAM(4-1)xCD3 (VH7/VL2)	LHHL
14	145	168	147	174	76	3	80	EPCAM(4-1)xCD3(VH7/VL2)	HLHL
15	147	168	145	174	80	3	76	EPCAM(4-1)xCD3 (VL2/ VH7)	LHLH
16	145	168	147	174	80	3	76	EPCAM(4-1)xCD3(VL2/ VH7)	HLLH

Table 3B

Deimmunized anti-human CD3 constructs comprising single chain anti-EpCAM 4-1 variable regions: nucleotide sequence

Construct	SEQ ID NO in construct portion ...							deimmunized anti-CD3 construct / Specificity (N -> C)	Domain Arrangement
	A	B	C	D	E	F	G		
1	79	202	73	175	144	201	146	CD3 (VL2/ VH5)xEPCAM(4-1)	LHHL
2	73	202	79	175	144	201	146	CD3 (VH5/VL2)xEPCAM(4-1)	HLHL
3	79	202	73	175	146	201	144	CD3 (VL2/ VH5)xEPCAM(4-1)	LHLH
4	73	202	79	175	146	201	144	CD3 (VH5/VL2)xEPCAM(4-1)	HLLH
5	146	201	144	173	73	202	79	EPCAM(4-1)xCD3 (VH5/VL2)	LHHL
6	144	201	146	173	73	202	79	EPCAM(4-1)xCD3 (VH5/VL2)	HLHL
7	146	201	144	173	79	202	73	EPCAM(4-1)xCD3 (VL2/ VH5)	LHLH
8	144	201	146	173	79	202	73	EPCAM(4-1)xCD3 (VL2/ VH5)	HLLH
9	79	202	75	175	144	201	146	CD3 (VL2/ VH7)xEPCAM(4-1)	LHHL
10	75	202	79	175	144	201	146	CD3 (VH7/VL2)xEPCAM(4-1)	HLHL
11	79	202	75	175	146	201	144	CD3 (VL2/ VH7)xEPCAM(4-1)	LHLH
12	75	202	79	175	146	201	144	CD3 (VH7/VL2)xEPCAM(4-1)	HLLH
13	146	201	144	173	75	202	79	EPCAM(4-1)xCD3 (VH7/VL2)	LHHL
14	144	201	146	173	75	202	79	EPCAM(4-1)xCD3 (VH7/VL2)	HLHL
15	146	201	144	173	79	202	75	EPCAM(4-1)xCD3 (VL2/ VH7)	LHLH
16	144	201	146	173	79	202	75	EPCAM(4-1)xCD3 (VL2/ VH7)	HLLH

Table 4A

Deimmunized anti-human CD3 constructs comprising single chain anti-EpCAM 4-7 variable regions: amino acid sequence

Construct	SEQ ID NO in construct portion ...							deimmunized anti-CD3 construct / Specificity (N -> C)	Domain Arrangement
	A	B	C	D	E	F	G		
1	80	3	74	176	149	168	151	CD3 (VL2/ VH5)xEPCAM(4-7)	LHHL
2	74	3	80	176	149	168	151	CD3 (VH5/VL2)xEPCAM(4-7)	HLHL
3	80	3	74	176	151	168	149	CD3 (VL2/ VH5)xEPCAM(4-7)	LHLH
4	74	3	80	176	151	168	149	CD3 (VH5/VL2)xEPCAM(4-7)	HLLH
5	151	168	149	174	74	3	80	EPCAM(4-7)xCD3 (VH5/VL2)	LHHL
6	149	168	151	174	74	3	80	EPCAM(4-7)xCD3(VH5/VL2)	HLHL
7	151	168	149	174	80	3	74	EPCAM(4-7)xCD3 (VL2/ VH5)	LHLH
8	149	168	151	174	80	3	74	EPCAM(4-7)xCD3(VL2/ VH5)	HLLH
9	80	3	76	176	149	168	151	CD3 (VL2/ VH7)xEPCAM(4-7)	LHHL
10	76	3	80	176	149	168	151	CD3 (VH7/VL2)xEPCAM(4-7)	HLHL
11	80	3	76	176	151	168	149	CD3 (VL2/ VH7)xEPCAM(4-7)	LHLH
12	76	3	80	176	151	168	149	CD3 (VH7/VL2)xEPCAM(4-7)	HLLH
13	151	168	149	174	76	3	80	EPCAM(4-7)xCD3 (VH7/VL2)	LHHL
14	149	168	151	174	76	3	80	EPCAM(4-7)xCD3(VH7/VL2)	HLHL
15	151	168	149	174	80	3	76	EPCAM(4-7)xCD3 (VL2/ VH7)	LHLH
16	149	168	151	174	80	3	76	EPCAM(4-7)xCD3(VL2/ VH7)	HLLH

Table 4B

Deimmunized anti-human CD3 constructs comprising single chain anti-EpCAM 4-7 variable regions: nucleotide sequence

Construct	SEQ ID NO in construct portion ...							deimmunized anti-CD3 construct / Specificity (N -> C)	Domain Arrangement
	A	B	C	D	E	F	G		
1	79	202	73	175	148	201	150	CD3 (VL2/ VH5)xEPCAM(4-7)	LHHL
2	73	202	79	175	148	201	150	CD3 (VH5/VL2)xEPCAM(4-7)	HLHL
3	79	202	73	175	150	201	148	CD3 (VL2/ VH5)xEPCAM(4-7)	LHLH
4	73	202	79	175	150	201	148	CD3 (VH5/VL2)xEPCAM(4-7)	HLLH
5	150	201	148	173	73	202	79	EPCAM(4-7)xCD3 (VH5/VL2)	LHHL
6	148	201	150	173	73	202	79	EPCAM(4-7)xCD3(VH5/VL2)	HLHL
7	150	201	148	173	79	202	73	EPCAM(4-7)xCD3 (VL2/ VH5)	LHLH
8	148	201	150	173	79	202	73	EPCAM(4-7)xCD3(VL2/ VH5)	HLLH
9	79	202	75	175	148	201	150	CD3 (VL2/ VH7)xEPCAM(4-7)	LHHL
10	75	202	79	175	148	201	150	CD3 (VH7/VL2)xEPCAM(4-7)	HLHL
11	79	202	75	175	150	201	148	CD3 (VL2/ VH7)xEPCAM(4-7)	LHLH
12	75	202	79	175	150	201	148	CD3 (VH7/VL2)xEPCAM(4-7)	HLLH
13	150	201	148	173	75	202	79	EPCAM(4-7)xCD3 (VH7/VL2)	LHHL
14	148	201	150	173	75	202	79	EPCAM(4-7)xCD3(VH7/VL2)	HLHL
15	150	201	148	173	79	202	75	EPCAM(4-7)xCD3 (VL2/ VH7)	LHLH
16	148	201	150	173	79	202	75	EPCAM(4-7)xCD3(VL2/ VH7)	HLLH

Table 5A

Deimmunized anti-human CD3 constructs comprising single chain anti-EpCAM 5-10 variable regions; amino acid sequence

Construct	SEQ ID NO in construct portion ...							deimmunized anti-CD3 construct / Specificity (N -> C)	Domain Arrangement
	A	B	C	D	E	F	G		
1	80	3	74	176	133	168	135	CD3 (VL2/ VH5)xEPCAM(5-10)	LHHL
2	74	3	80	176	133	168	135	CD3 (VH5/VL2)xEPCAM(5-10)	HLHL
3	80	3	74	176	135	168	133	CD3 (VL2/ VH5)xEPCAM(5-10)	LHLH
4	74	3	80	176	135	168	133	CD3 (VH5/VL2)xEPCAM(5-10)	HLLH
5	135	168	133	174	74	3	80	EPCAM(5-10)xCD3 (VH5/VL2)	LHHL
6	133	168	135	174	74	3	80	EPCAM(5-10)xCD3(VH5/VL2)	HLHL
7	135	168	133	174	80	3	74	EPCAM(5-10)xCD3 (VL2/ VH5)	LHLH
8	133	168	135	174	80	3	74	EPCAM(5-10)xCD3(VL2/ VH5)	HLLH
9	80	3	76	176	133	168	135	CD3(VL2/ VH7) xEPCAM(5-10)	LHHL
10	76	3	80	176	133	168	135	CD3 (VH7/VL2) xEPCAM(5-10)	HLHL
11	80	3	76	176	135	168	133	CD3(VL2/VH7) xEPCAM(5-10)	LHLH
12	76	3	80	176	135	168	133	CD3 (VH7/VL2) xEPCAM(5-10)	HLLH
13	135	168	133	174	76	3	80	EPCAM(5-10)xCD3 (VH7/VL2)	LHHL
14	133	168	135	174	76	3	80	EPCAM(5-10)xCD3(VH7/VL2)	HLHL
15	135	168	133	174	80	3	76	EPCAM(5-10)xCD3 (VL2/ VH7)	LHLH
16	133	168	135	174	80	3	76	EPCAM(5-10)xCD3(VL2/ VH7)	HLLH

Table 5B

Deimmunized anti-human CD3 constructs comprising single chain anti-EpCAM 5-10 variable regions: nucleotide sequence

Construct	SEQ ID NO in construct portion ...							deimmunized anti-CD3 construct / Specificity (N -> C)	Domain Arrangement
	A	B	C	D	E	F	G		
1	79	202	73	175	132	201	134	CD3 (VL2/ VH5) xEPCAM(5-10)	LHHL
2	73	202	79	175	132	201	134	CD3 (VH5/VL2) xEPCAM(5-10)	HLHL
3	79	202	73	175	134	201	132	CD3 (VL2/ VH5) xEPCAM(5-10)	LHLH
4	73	202	79	175	134	201	132	CD3 (VH5/VL2) xEPCAM(5-10)	HLLH
5	134	201	132	173	73	202	79	EPCAM(5-10)xCD3 (VH5/VL2)	LHHL
6	132	201	134	173	73	202	79	EPCAM(5-10)xCD3(VH5/VL2)	HLHL
7	134	201	132	173	79	202	73	EPCAM(5-10)xCD3 (VL2/ VH5)	LHLH
8	132	201	134	173	79	202	73	EPCAM(5-10)xCD3(VL2/ VH5)	HLLH
9	79	202	75	175	132	201	134	CD3 (VL2/ VH7) xEPCAM(5-10)	LHHL
10	75	202	79	175	132	201	134	CD3 (VH7/VL2) xEPCAM(5-10)	HLHL
11	79	202	75	175	134	201	132	CD3 (VL2/ VH7) xEPCAM(5-10)	LHLH
12	75	202	79	175	134	201	132	CD3 (VH7/VL2) xEPCAM(5-10)	HLLH
13	134	201	132	173	75	202	79	EPCAM(5-10)xCD3 (VH7/VL2)	LHHL
14	132	201	134	173	75	202	79	EPCAM(5-10)xCD3(VH7/VL2)	HLHL
15	134	201	132	173	79	202	75	EPCAM(5-10)xCD3 (VL2/ VH7)	LHLH
16	132	201	134	173	79	202	75	EPCAM(5-10)xCD3(VL2/ VH7)	HLLH

Most preferably, the invention provides bispecific antibody constructs comprising a specificity binding to CD3 and EpCAM and having the SEQ ID NO.:30, 31 (construct 2 of Table 1A and 1B), Seq ID NO.: 48, 49 (construct 5 of the Table 1A, 1B), SEQ ID NO.: 64, 65 (construct 2 of Table 2A, 2B), SEQ ID NO: 54, 55 (construct 5 of Table 2A, 2B), Seq ID NO.: 66, 67 (construct 2 of Table 3A, 3B), SEQ ID NO.: 32, 33 (construct 2 of Table 4A, 4B), SEQ ID NO.:34, 35 (construct 4 of Table 4A, 4B), SEQ ID NO.: 60, 61 (construct 5 of Table 4A, 4B), SEQ ID NO.: 36, 37 (construct 2 of Table 5A, 5B), SEQ ID NO.: 38, 39 (construct 4 of Table 5A, 5B) or SEQ ID NO.:62, 63 (construct 5 of Table 5A, 5B).

10

In accordance with constructs provided herein above, particularly preferred CD3 and EpCAM binding constructs of the invention, comprising at least the above described first domain with reduced propensity for T cell epitope generation and specificity for human CD3 and a second, Ig-derived domain which is specific for EpCAM are shown in SEQ ID NOs.: 31, 33, 35, 37, 39, 49, 55, 58, 61, 63, 65, 67, 237, 239, 241, 243, 245, 247, 249, 251, 253, 255, 257, 259, 261, 263, 265, 267, 269, 271, 273, 275, 277, 279, 281, 283, 285, 287, 289, 291, 293, 295, 297, 299, 301, 303, 305, 307, 309, 311, 313, 315, 317, 319, 321, 323 and 325. Corresponding nucleic acid molecules encoding said preferred CD3 and EpCAM binding constructs as defined herein comprise SEQ ID NOs: 30, 32, 34, 36, 38, 48, 54, 57, 60, 62, 64, 66, 236, 238, 240, 242, 244, 246, 248, 250, 252, 254, 256, 258, 260, 262, 264, 266, 268, 270, 272, 274, 276, 278, 280, 282, 284, 286, 288, 290, 292, 294, 296, 298, 300, 302, 304, 306, 308, 310, 312, 314, 316, 318, 320, 322 and 324.

Accordingly, the present invention also provides for CD3 specific binding constructs comprising a first domain which specifically binds to human CD3 and has reduced propensity to generate T cell epitopes and comprising an Ig-derived second domain directed against/ capable of binding to EpCAM, selected from the group consisting of

(a) an amino acid sequence as shown in any one of SEQ ID NO 31, 33, 35, 37, 39, 49, 55, 58, 61, 63, 65, 67, 237, 239, 241, 243, 245, 247, 249, 251, 253, 255, 257, 259, 261, 263, 265, 267, 269, 271, 273, 275, 277, 279, 281, 283, 285, 287, 289, 291, 293, 295, 297, 299, 301, 303, 305, 307, 309, 311, 313, 315, 317, 319, 321, 323 or 325;

30

- (b) an amino acid sequence encoded by a nucleic acid sequence as shown in any one of SEQ ID NO 30, 32, 34, 36, 38, 48, 54, 57, 60, 62, 64, 66, 236, 238, 240, 242, 244, 246, 248, 250, 252, 254, 256, 258, 260, 262, 264, 266, 268, 270, 272, 274, 276, 278, 280, 282, 284, 286, 288, 290, 292, 294, 296, 298, 300, 302, 304, 306, 308, 310, 312, 314, 316, 318, 320, 322 or 324;
- (c) an amino acid sequence encoded by a nucleic acid sequence which is degenerate as a result of the genetic code to a nucleotide sequence of (b);
- (d) an amino acid sequence encoded by a nucleic acid sequence hybridizing with the complementary strand of a nucleic acid sequence as defined in (b) under stringent hybridization conditions;

The present invention also provides for CD3 specific binding constructs comprising a first domain which specifically binds to human CD3 and has reduced propensity to generate T cell epitopes and comprising an Ig-derived second domain directed against/ capable of binding to EpCAM, which comprise an amino acid sequence encoded by a nucleic acid sequence hybridizing with the complementary strand of a nucleic acid sequence as defined in (b) herein above, i.e. to a nucleic acid sequence as shown in any one of SEQ ID NO 30, 32, 34, 36, 38, 48, 54, 57, 60, 62, 64, 66, 236, 238, 240, 242, 244, 246, 248, 250, 252, 254, 256, 258, 260, 262, 264, 266, 268, 270, 272, 274, 276, 278, 280, 282, 284, 286, 288, 290, 292, 294, 296, 298, 300, 302, 304, 306, 308, 310, 312, 314, 316, 318, 320, 322 or 324 under stringent hybridization conditions.

The term "hybridizing" as used herein refers to polynucleotides/nucleic acid sequences which are capable of hybridizing to the polynucleotides encoding the deimmunized constructs as defined herein. Therefore, said polynucleotides may be useful as probes in Northern or Southern Blot analysis of RNA or DNA preparations, respectively, or can be used as oligonucleotide primers in PCR analysis dependent on their respective size. Preferably, said hybridizing polynucleotides comprise at least 10, more preferably at least 15 nucleotides in length while a hybridizing polynucleotide of the present invention to be used as a probe preferably comprises at least 100, more preferably at least 200, or most preferably at least 500 nucleotides in length.

It is well known in the art how to perform hybridization experiments with nucleic acid molecules, i.e. the person skilled in the art knows what hybridization conditions s/he has to use in accordance with the present invention. Such hybridization conditions

are referred to in standard text books such as Molecular Cloning A Laboratory Manual, Cold Spring Harbor Laboratory (2001) N.Y. Preferred in accordance with the present inventions are polynucleotides which are capable of hybridizing to the polynucleotides of the invention or parts thereof, under stringent hybridization conditions.

"Stringent hybridization conditions" refer, i.e. to an overnight incubation at 42°C in a solution comprising 50% formamide, 5x SSC (750 mM NaCl, 75 mM sodium citrate), 50 mM sodium phosphate (pH 7.6), 5x Denhardt's solution, 10% dextran sulfate, and 20 µg/ml denatured, sheared salmon sperm DNA, followed by washing the filters in 0.1 x SSC at about 65°C. Also contemplated are nucleic acid molecules that hybridize to the polynucleotides of the invention at lower stringency hybridization conditions. Changes in the stringency of hybridization and signal detection are primarily accomplished through the manipulation of formamide concentration (lower percentages of formamide result in lowered stringency); salt conditions, or temperature. For example, lower stringency conditions include an overnight incubation at 37°C in a solution comprising 6X SSPE (20X SSPE = 3M NaCl; 0.2M NaH₂PO₄; 0.02M EDTA, pH 7.4), 0.5% SDS, 30% formamide, 100 µg/ml salmon sperm blocking DNA; followed by washes at 50°C with 1 X SSPE, 0.1% SDS. In addition, to achieve even lower stringency, washes performed following stringent hybridization can be done at higher salt concentrations (e.g. 5X SSC). It is of note that variations in the above conditions may be accomplished through the inclusion and/or substitution of alternate blocking reagents used to suppress background in hybridization experiments. Typical blocking reagents include Denhardt's reagent, BLOTTO, heparin, denatured salmon sperm DNA, and commercially available proprietary formulations. The inclusion of specific blocking reagents may require modification of the hybridization conditions described above, due to problems with compatibility.

The recited nucleic acid molecules may be, e.g., DNA, cDNA, RNA or synthetically produced DNA or RNA or a recombinantly produced chimeric nucleic acid molecule comprising any of those polynucleotides either alone or in combination.

The deimmunized CD3 and EpCAM binding constructs provided in this invention are particularly useful in medical settings, for example in the prevention, treatment and/or the amelioration of tumorous diseases, in particular, breast cancer, colon cancer, prostate cancer, head and neck cancer, skin cancer (melanoma), cancers of the

genito-urinary tract, e.g. ovarian cancer, endometrial cancer, cervix cancer and kidney cancer, lung cancer, gastric cancer, cancer of the small intestine, liver cancer, pancreas cancer, gall bladder cancer, cancers of the bile duct, esophagus cancer, cancer of the salivatory glands and cancer of the thyroid gland. In particular, the
 5 deimmunized constructs binding CD3 and EpCAM can be used for the treatment of epithelial cancer, preferably adenocarcinomas, or minimal residual disease, more preferably early solid tumor, advanced solid tumor or metastatic solid tumor.

10 In a more particularly preferred embodiment of the CD3 specific binding construct described herein, said construct comprises a second Ig-derived domain which comprises an antigen-interaction site with a specificity CCR5.

The chemokine receptor CCR5 is a member of a large family of G protein coupled seven transmembrane domain receptors that binds the proinflammatory chemokines RANTES, MIP1- α , MIP1- β and MCP-2. Chemokines act in concert with adhesion
 15 molecules to induce the extravasation of leukocytes and to direct their migration to sites of tissue injury. CCR5 is expressed on a minority of T-cells and monocytes and is further the major co-receptor for M-trophic HIV-1 strains that predominate early in the course of an HIV-infection.

Human immunodeficiency virus (HIV) cannot enter human cells unless it first binds to
 20 two key molecules on the cell surface, CD4 and a co-receptor. The co-receptor that is initially recognized is CCR5, later in the life cycle of the virus another chemokine receptor CXCR4 becomes the co-receptor for HIV-1 (D'Souza, Nature Med. 2, 1293 (1996); Premack, Nature Med. 2, 1174; Fauci, Nature 384, 529 (1996)). The HIV-1 strains that cause most transmissions of viruses by sexual contact are called M-tropic
 25 viruses. These HIV-1 strains (also known as non-syncytia inducing (NSI) primary viruses) can replicate in primary CD4+ T-cells and macrophages and use the chemokine receptor CCR5 (and, less often, CCR3) as their coreceptor. The T-tropic viruses (sometimes called syncytia inducing (SI) primary viruses) can also replicate in primary CD4+ T-cells but can in addition infect established CD4+ T-cell lines in
 30 vitro, which they do via the chemokine receptor CXCR4 (fusin). Many of these T-tropic strains can use CCR5 in addition to CXCR4, and some can enter macrophages via CCR5, at least under certain in vitro conditions (D'Souza, Nature Med. 2, 1293 (1996); Premack, Nature Med. 2, 1174; Fauci, Nature 384, 529 (1996)). Whether other coreceptors contribute to HIV-1 pathogenesis is unresolved, but the

existence of another coreceptor for some T-tropic strains can be inferred from in vitro studies. Because M-tropic HIV-1 strains are implicated in about 90% of sexual transmissions of HIV, CCR5 is the predominant coreceptor for the virus in patients; transmission (or systemic establishment) of CXCR4-using (T-tropic) strains is rare.

5 (D'Souza, *Nature Med.* 2, 1293 (1996); Premack, *Nature Med.* 2, 1174; Fauci, *Nature* 384, 529 (1996), Paxton, *Nature Med.* 2, 412 (1996); Liu, *Cell* 86, 367 (1996); Samson, *Nature* 382, 722 (1996); Dean, *Science* 273, 1856 (1996); Huang, *Nature Med.* 2, 1240 (1996)). However, once SI viruses evolve in vivo (or if they are transmitted), they are especially virulent and cause faster disease progression.

10 (D'Souza, *Nature Med.* 2, 1293 (1996); Premack, *Nature Med.* 2, 1174; Fauci, *Nature* 384, 529 (1996), Schuitemaker, *J. Virol.* 66, 1354 (1992); Connor, *J. Virol.* 67, 1772 (1993); Richman, *J. Infect. Dis.* 169, 968 (1994); R. I. Connor et al., *J. Exp. Med.* 185, 621 (1997); Trkola, *Nature* 384, 184 (1996)).

The numbers and identity of coreceptor molecules on target cells, and the ability of HIV-1 strains to likely enter cells via the different coreceptors, seem to be critical determinants of disease progression. These factors are major influences on both host- and virus-dependent aspects of HIV-1 infection. For example, a homozygous defect (delta 32) in CCR5 correlates strongly with resistance to HIV-1 infection in vivo and in vitro. Individuals who are heterozygous for a defective CCR5 allele are at best

15 weakly protected against infection and have only a modestly slowed disease progression (Paxton, *Nature Med.* 2, 412 (1996); Liu, *Cell* 86, 367 (1996); Samson, *Nature* 382, 722 (1996); Dean, *Science* 273, 1856 (1996); Huang et al., *Nature Med.* 2, 1240 (1996)). However, other factors can influence the level of CCR5 expression on activated CD4+ T-cells and thereby affect the efficiency of HIV-1 infection in vitro

20 (Trkola, *Nature* 384, 184 (1996); Bleul, *Proc. Natl. Acad. Sci. U.S.A.* 94, 1925 (1997)).

For multiple sclerosis it was shown that CCR5 and CXCR3 are predominantly expressed on T-cells infiltrating demyelinating brain lesions, as well as in the peripheral blood of affected patients. Elimination of the T-cells would block the T-cell

30 arm of this autoimmune disease.

High expression of CCR3 and CCR5 was also observed in T cells and B cells of lymph nodes derived from patients with Hodgkin's disease.

Diabetes type I is considered to be a T-cell mediated autoimmune disease. The expression of CCR5 receptor in the pancreas was associated with the progression of

type I diabetes in relevant animal models (Cameron (2000) J. Immunol. 165, 1102-1110). In particular, the CCR5 expression was associated with the development of insulinitis and spontaneous type I diabetes.

Several antibodies specifically binding to (human) CCR5 are known in the art and comprise, MC-1 (Mack (1998) J. Exp. Med. 187, 1215-1224 or MC-5 (Blanpain (2002) Mol Biol Cell. 13:723-37, Segerer (1999) Kidney Int. 56:52-64, Kraft (2001) J Biol Chem. 14;276:34408-18). The CCR-5 antibodies, in particular MC-1 and MC-5 may serve as a source for Ig-derived second domain of the CD3 specific construct of the invention. Accordingly, in a preferred embodiment, the invention relates to a bispecific construct comprising at least two domains, wherein the first domain provides for the specificity to human CD3 and has a reduced propensity to generate T cell epitopes and whereby said Ig-derived second domain is derived from an antibody specific for (human) CCR5. Most preferably, such a construct is a single chain scFV as defined herein .

MC-1 was shown to bind specifically to the first part of the second extracellular loop of human CCR5 and did not crossreact with CCR5 derived from rhesus macaques as shown in the appended examples. Therefore, it is preferred that the CD3 specific construct of this invention comprises, for example, VL and VH domains of an antibody (i.e. an Ig-derived second domain) specific for CCR5, preferably the human CCR5, and VH and VL domains of an antibody specific for the CD3 antigen. Said antibody specific for the human CCR5 is the murine anti-human CCR5 antibody MC-1, described, inter alia, in Mack (1998), J. Exp. Med. 187, 1215-1224 and in the appended examples. Yet, it is envisaged that other α -CCR5 antibodies, like MC-5 (as characterized in the appended examples and disclosed in Blanpain (2002) Mol Biol Cell. 13:723-37, Segerer (1999) Kidney Int. 56:52-64 and Kraft (2001) J Biol Chem. 14;276:34408-18 may be employed in the context of this invention.

In a particularly preferred embodiment of the present invention, CD3-specific binding constructs are provided, which comprise a deimmunized domain directed against/binding to/interacting with human CD3 and a second Ig-derived domain which specifically binds to/interacts with CCR5. Such constructs are shown in Table 6A and 6B. The modules A-G in Tables 6A and 6B can be defined as mentioned above for Tables 1-5. Deimmunized VH domains of antibodies having specificity for the human CD3 antigen can be selected from the sequences as set out in SEQ ID

NOs: 74 or 76. Deimmunized VL domains of antibodies having specificity for the human CD3 antigen can be selected from the sequences as set out in SEQ ID NOs: 78, 80 or 82. The VH protein domain of human CCR5 antibody is as set out in SEQ ID NO: 129. The VL protein domain of human CCR5 antibody is as set out in SEQ ID NO: 131. When either the module pair A/C or E/G is a pair of deimmunized VH/VL or VL/VH protein domains from an antibody having specificity for the human CD3 antigen, protein module B or F, respectively, has the amino acid sequence as set out in SEQ ID NO: 3. When either the module pair A/C or E/G is a pair of VH/VL or VL/VH from an antibody having specificity for the EpCAM antigen, protein module B or F, respectively, has the amino acid sequence as set out in SEQ ID NO: 168. The respective groups of protein modules A-B-C and E-F-G are connected to each other through protein module D, having the sequence as set out in SEQ ID NO: 174. However, as mentioned above an additional serine may be introduced for cloning purposes (linker as depicted in SEQ ID NO.:176) between the VL and subsequent V domain.

Nucleic acid molecules encoding deimmunized VH domains of antibodies having specificity for the human CD3 antigen can be selected from the sequences as set out in SEQ ID NOs: 73 or 75. Nucleic acid molecules encoding deimmunized VL domains of antibodies having specificity for the human CD3 antigen can be selected from the sequences as set out in SEQ ID NOs: 77, 79 or 81. The nucleic acid molecule encoding the VH protein domain of the human CCR5 antibody is as set out in SEQ ID NO: 128. The nucleic acid molecule encoding the VL protein domain of the human CCR5 antibody is as set out in SEQ ID NO: 130. When either the module pair A/C or E/G denotes nucleic acid encoding a pair of deimmunized VH/VL or VL/VH protein domains from an antibody having specificity for the human CD3 antigen, nucleic acid module B or F, respectively, has the nucleic acid sequence as set out in SEQ ID NO: 202. When either the module pair A/C or E/G denotes nucleic acid encoding a pair of VH/VL or VL/VH from an antibody having specificity for the CCR5 antigen, nucleic acid module B or F, respectively, has the nucleic acid sequence as set out in SEQ ID NO: 201. The groups of nucleic acid modules A-B-C and E-F-G are connected to each other through protein module D, having the sequence as set out in SEQ ID NO: 173. An alternative linker SEQ ID NO.:175 may also be used to conjugate VL domain with a subsequent V domain (including an additional codon encoding a serine residue for cloning purposes).

Table 6A Deimmunized anti-human CD3 constructs comprising single chain anti-CCR5 variable regions: amino acid sequence

Construct	SEQ ID NO in construct portion ...							deimmunized anti-CD3 construct / Specificity (N -> C)	Domain Arrangement
	A	B	C	D	E	F	G		
1	80	3	74	174	129	168	131	CD3 (VL2/ VH5) xCCR5	LHHL
2	74	3	80	174	129	168	131	CD3 (VH5/VL2) xCCR5	HLHL
3	80	3	74	174	131	168	129	CD3 (VL2/ VH5) xCCR5	LHLH
4	74	3	80	174	131	168	129	CD3 (VH5/VL2) xCCR5	HLLH
5	131	168	129	174	74	3	80	CCR5xCD3 (VH5/VL2)	LHHL
6	129	168	131	174	74	3	80	CCR5xCD3(VH5/VL2)	HLHL
7	131	168	129	174	80	3	74	CCR5xCD3 (VL2/ VH5)	LHLH
8	129	168	131	174	80	3	74	CCR5xCD3(VL2/ VH5)	HLLH
9	80	3	76	174	129	168	131	CD3 (VL2/ VH7) xCCR5	LHHL
10	76	3	80	174	129	168	131	CD3 (VH7/VL2) xCCR5	HLHL
11	80	3	76	174	131	168	129	CD3 (VL2/ VH7) xCCR5	LHLH
12	76	3	80	174	131	168	129	CD3 (VH7/VL2) xCCR5	HLLH
13	131	168	129	174	76	3	80	CCR5xCD3 (VH7/VL2)	LHHL
14	129	168	131	174	76	3	80	CCR5xCD3(VH7/VL2)	HLHL
15	131	168	129	174	80	3	76	CCR5xCD3 (VL2/ VH7)	LHLH
16	129	168	131	174	80	3	76	CCR5xCD3(VL2/ VH7)	HLLH

Table 6B Deimmunized anti-human CD3 constructs comprising single chain anti-CCR5 variable regions: nucleic acid sequence

Construct	SEQ ID NO in construct portion ...							deimmunized anti-CD3 construct / Specificity (N -> C)	Domain Arrangement
	A	B	C	D	E	F	G		
1	79	202	73	173	128	201	130	CD3 (VL2/ VH5) xCCR5	LHHL
2	73	202	79	173	128	201	130	CD3 (VH5/VL2) xCCR5	HLHL
3	79	202	73	173	130	201	128	CD3 (VL2/ VH5) xCCR5	LHLH
4	73	202	79	173	130	201	128	CD3 (VH5/VL2) xCCR5	HLLH
5	130	201	128	173	73	202	79	CCR5xCD3 (VH5/VL2)	LHHL
6	128	201	130	173	73	202	79	CCR5xCD3(VH5/VL2)	HLHL
7	130	201	128	173	79	202	73	CCR5xCD3 (VL2/ VH5)	LHLH
8	128	201	130	173	79	202	73	CCR5xCD3(VL2/ VH5)	HLLH
9	79	202	75	173	128	201	130	CD3 (VL2/ VH7) xCCR5	LHHL
10	75	202	79	173	128	201	130	CD3 (VH7/VL2) xCCR5	HLHL
11	79	202	75	173	130	201	128	CD3 (VL2/ VH7) xCCR5	LHLH
12	75	202	79	173	130	201	128	CD3 (VH7/VL2) xCCR5	HLLH
13	130	201	128	173	75	202	79	CCR5xCD3 (VH7/VL2)	LHHL
14	128	201	130	173	75	202	79	CCR5xCD3(VH7/VL2)	HLHL
15	130	201	128	173	79	202	75	CCR5xCD3 (VL2/ VH7)	LHLH
16	128	201	130	173	79	202	75	CCR5xCD3 (VL2/ VH7)	HLLH

Preferably, said constructs comprise an amino acid sequence selected from the group of

- (a) an amino acid sequence as shown in any one of SEQ ID NO 206, 208, 210, 212, 214 or 216;
- 5 (b) an amino acid sequence encoded by a nucleic acid sequence as shown in any one of in SEQ ID NO 205, 207, 209, 211, 213 or 215; and
- (c) an amino acid sequence encoded by a nucleic acid sequence which is degenerate as a result of the genetic code to a nucleotide sequence of (b);
- 10 (d) and amino acid sequence encoded by a nucleic acid sequence hybridising with the complementary strand of a nucleic acid sequence as defined in (b) under stringent hybridisation conditions.

The CCR5 and CD3 binding constructs 206, 208, 210 represent construct 5 and SEQ ID NO.:212, 214 and 216 represent construct 13 of Table 6 and have the three
15 different VL regions (VL1 (SEQ ID NO.:78), VL2 (SEQ ID NO.:80), or VL3 (SEQ ID NO.:82)).

The present invention also provides for CD3 specific binding constructs comprising a first domain which specifically binds to human CD3 and has reduced propensity to
20 generate T cell epitopes and comprising an Ig-derived second domain directed against/ capable of binding to CCR5, which comprise an amino acid sequence encoded by a nucleic acid sequence hybridizing with the complementary strand of a nucleic acid sequence as defined in (b) herein above, i.e. to a nucleic acid sequence as shown in any one of SEQ ID NO 205, 207, 209, 211, 213 or 215 under stringent
25 hybridization conditions. The terms "hybridization" and "stringent conditions" have been described herein above. The corresponding definitions and embodiments apply here mutatis mutandis.

The deimmunized CD3 and CCR5 binding constructs provided herein are particularly
30 useful in the medical intervention of viral disease, in particular HIV infections and AIDS, or of autoimmune diseases and/or inflammatory diseases, like rheumatoid arthritis.

In another embodiment, the present invention provides for CD3 specific binding constructs as defined herein above, wherein the Ig-derived second domain of the inventive construct comprises an antigen-interaction site with specificity for CD19.

5 CD19 has proved to be a very useful medical target. CD19 is expressed in the whole B lineage from the pro B cell to the mature B cell, it is not shed, is uniformly expressed on all lymphoma cells, and is absent from stem cells (Haagen, Clin Exp Immunol 90 (1992), 368-75; Uckun, Proc. Natl. Acad. Sci. USA 85 (1988), 8603-7). Combination therapy employing both an antibody directed against CD19 and an
10 additional immunoregulatory antibody has been disclosed for the treatment of B cell malignancies (WO 02/04021, US2002006404, US2002028178) and autoimmune diseases (WO 02/22212, US2002058029). WO 00/67795 discloses the use i.a. of antibodies directed against CD19 for the treatment of indolent and aggressive forms of B-cell lymphomas, as well as acute and chronic forms of lymphatic leukemias. WO
15 02/80987 discloses the therapeutic use of immunotoxins based on antibodies against the antigen CD19 for the treatment of such diseases as B cell non-Hodgkin's lymphoma, Hodgkin's lymphoma or B cell leukemias (e.g. B cell acute lymphatic leukemia (B-ALL), (e.g. hairy cell lymphoma) B cell precursor acute lymphatic leukemia (pre-B-ALL), B cell chronic lymphatic leukemia (B-CLL)) .

20

In a particularly preferred embodiment of the present invention, CD3-specific binding constructs are provided, which comprise an deimmunized domain directed against/binding to/interacting with human CD3 and a second Ig-derived domain which specifically binds to/interacts with CD19. Such constructs are shown in Table
25 7A and 7B. The modules A-G in Tables 7A and 7B can be defined as mentioned above for Tables 1-5. Deimmunized VH domains of antibodies having specificity for the human CD3 antigen can be selected from the sequences as set out in SEQ ID NOs: 74 or 76. Deimmunized VL domains of antibodies having specificity for the human CD3 antigen can be selected from the sequences as set out in SEQ ID NOs:
30 78, 80 or 82. The VH protein domain of human CD19 antibody is as set out in SEQ ID NO: 114. The VL protein domain of human CCR5 antibody is as set out in SEQ ID NO: 116. When either the module pair A/C or E/G is a pair of deimmunized VH/VL or VL/VH protein domains from an antibody having specificity for the human CD3 antigen, protein module B or F, respectively, has the amino acid sequence as set out

- in SEQ ID NO: 3. When either the module pair A/C or E/G is a pair of VH/VL or VL/VH from an antibody having specificity for the CD19 antigen, protein module B or F, respectively, has the amino acid sequence as set out in SEQ ID NO: 168. The respective groups of protein modules A-B-C and E-F-G are connected to each other through protein module D, having the sequence as set out in SEQ ID NO: 174. However, as mentioned above an additional serine may be introduced for cloning purposes (linker as depicted in SEQ ID NO.:176) between the VL and subsequent V domain.
- 10 Nucleic acid molecules encoding deimmunized VH domains of antibodies having specificity for the human CD3 antigen can be selected from the sequences as set out in SEQ ID NOs: 73 or 75. Nucleic acid molecules encoding deimmunized VL domains of antibodies having specificity for the human CD3 antigen can be selected from the sequences as set out in SEQ ID NOs: 77, 79 or 81. The nucleic acid molecule encoding the VH protein domain of the human CD19 antibody is as set out in SEQ ID NO: 113. The nucleic acid molecule encoding the VL protein domain of the human CCR5 antibody is as set out in SEQ ID NO: 115. When either the module pair A/C or E/G denotes nucleic acid encoding a pair of deimmunized VH/VL or VL/VH protein domains from an antibody having specificity for the human CD3 antigen, nucleic acid module B or F, respectively, has the amino acid sequence as set out in SEQ ID NO: 202. When either the module pair A/C or E/G denotes a nucleic acid encoding a pair of VH/VL or VL/VH from an antibody having specificity for the CD19 antigen, nucleic acid module B or F, respectively, has the nucleic acid sequence as set out in SEQ ID NO: 201. The groups of nucleic acid modules A-B-C and E-F-G are connected to each other through protein module D, having the sequence as set out in SEQ ID NO: 173. An alternative linker SEQ ID NO.:175 may also be used to conjugate VL domain with a subsequent V domain (including an additional codon encoding a serine residue for cloning purposes).

Table 7A Deimmunized anti-human CD3 constructs comprising single chain anti-CD19 variable regions: amino acid sequence

Construct	SEQ ID NO in construct portion ...							deimmunized anti-CD3 construct / Specificity (N -> C)	Domain Arrangement
	A	B	C	D	E	F	G		
1	80	3	74	174	114	168	116	CD3 (VL2/ VH5) xCD19	LHHL
2	74	3	80	174	114	168	116	CD3 (VH5/VL2) xCD19	HLHL
3	80	3	74	174	116	168	114	CD3 (VL2/ VH5) xCD19	LHLH
4	74	3	80	174	116	168	114	CD3 (VH5/VL2) xCD19	HLLH
5	116	168	114	174	74	3	80	CD19xCD3 (VH5/VL2)	LHHL
6	114	168	116	174	74	3	80	CD19xCD3(VH5/VL2)	HLHL
7	116	168	114	174	80	3	74	CD19xCD3 (VL2/ VH5)	LHLH
8	114	168	116	174	80	3	74	CD19xCD3(VL2/ VH5)	HLLH
9	80	3	76	174	114	168	116	CD3 (VL2/ VH7) xCD19	LHHL
10	76	3	80	174	114	168	116	CD3 (VH7/VL2) xCD19	HLHL
11	80	3	76	174	116	168	114	CD3 (VL2/ VH7) xCD19	LHLH
12	76	3	80	174	116	168	114	CD3 (VH7/VL2) xCD19	HLLH
13	116	168	114	174	76	3	80	CD19xCD3 (VH7/VL2)	LHHL
14	114	168	116	174	76	3	80	CD19xCD3(VH7/VL2)	HLHL
15	116	168	114	174	80	3	76	CD19xCD3 (VL2/ VH7)	LHLH
16	114	168	116	174	80	3	76	CD19xCD3(VL2/ VH7)	HLLH

Table 7B Deimmunized anti-human CD3 constructs comprising single chain anti-CD19 variable regions: Nucleic acid sequence

Construct	SEQ ID NO in construct portion ...							deimmunized anti-CD3 construct / Specificity (N -> C)	Domain Arrangement
	A	B	C	D	E	F	G		
1	79	202	73	173	113	201	115	CD3 (VL2/ VH5) xCD19	LHHL
2	73	202	79	173	113	201	115	CD3 (VH5/VL2) xCD19	HLHL
3	79	202	73	173	115	201	113	CD3 (VL2/ VH5) xCD19	LHLH
4	73	202	79	173	115	201	113	CD3 (VH5/VL2) xCD19	HLLH
5	115	201	113	173	73	202	79	CD19xCD3 (VH5/VL2)	LHHL
6	113	201	115	173	73	202	79	CD19xCD3(VH5/VL2)	HLHL
7	115	201	113	173	79	202	73	CD19xCD3 (VL2/ VH5)	LHLH
8	113	201	115	173	79	202	73	CD19xCD3(VL2/ VH5)	HLLH
9	79	202	75	173	113	201	115	CD3 (VL2/ VH7) xCD19	LHHL
10	75	202	79	173	113	201	115	CD3 (VH7/VL2) xCD19	HLHL
11	79	202	75	173	115	201	113	CD3 (VL2/ VH7) xCD19	LHLH
12	75	202	79	173	115	201	113	CD3 (VH7/VL2) xCD19	HLLH
13	115	201	113	173	75	202	79	CD19xCD3 (VH7/VL2)	LHHL
14	113	201	115	173	75	202	79	CD19xCD3(VH7/VL2)	HLHL
15	115	201	113	173	79	202	75	CD19xCD3 (VL2/ VH7)	LHLH
16	113	201	115	173	79	202	75	CD19xCD3(VL2/ VH7)	HLLH

In a more preferred embodiment, the present invention provides for a deimmunized CD3-specific binding construct which comprises a CD3-binding domain as defined above and a second, Ig-derived domain which specifically binds to /interacts with CD19, preferably human CD19, wherein said CD3-specific binding construct
 5 comprises an amino acid sequence selected from the group of

- (a) an amino acid sequence as shown in any one of SEQ ID NO 190, 192, 194, 196, 198, 200, 327, 329, 331, 333, 335, 337, 339, 341, 343, 345, 347, 349, 351, 353, 357, 359, 361, 363, 365, 367, 369, 371, 373, 375, 377, 379, 381, 383, 385, 387, 389, 391, 393, 395, 397, 399, 401, 403, 405, 407 or 409;
- 10 (b) an amino acid sequence encoded by a nucleic acid sequence as shown in any one of in SEQ ID NO 189, 191, 193, 195, 197, 199, 326, 328, 330, 332, 334, 336, 338, 340, 342, 344, 346, 348, 350, 352, 354, 356, 358, 360, 362, 364, 366, 368, 370, 372, 374, 376, 378, 380, 382, 384, 386, 388, 390, 392, 394, 396, 398, 400, 402, 404, 406 or 408; and
- 15 (c) an amino acid sequence encoded by a nucleic acid sequence which is degenerate as a result of the genetic code to a nucleotide sequence of (b);
- (d) and amino acid sequence encoded by a nucleic acid sequence hybridising with the complementary strand of a nucleic acid sequence as defined in (b) under stringent hybridisation conditions.

20 Preferred CD19 and CD3 binding constructs according to the invention are SEQ ID NO.:190, 192, 194 representing construct 5 and SEQ ID NO.:196, 198 and 200 representing construct 13 of Table 7 and having the three different VL regions (VL1 (SEQ ID NO.:78), VL2 (SEQ ID NO.:80), or VL3 (SEQ ID NO.:82)).

25 The present invention also provides for CD3 specific binding constructs comprising a first domain which specifically binds to human CD3 and has reduced propensity to generate T cell epitopes and comprising an Ig-derived second domain directed against/ capable of binding to CD19, which comprise an amino acid sequence
 30 encoded by a nucleic acid sequence hybridizing with the complementary strand of a nucleic acid sequence as defined in (b) herein above, i.e. to a nucleic acid sequence as shown in any one of SEQ ID NOs: 189, 191, 193, 195, 197, 199, 326, 328, 330, 332, 334, 336, 338, 340, 342, 344, 346, 348, 350, 352, 354, 356, 358, 360, 362, 364, 366, 368, 370, 372, 374, 376, 378, 380, 382, 384, 386, 388, 390, 392, 394, 396, 398,

400, 402, 404, 406 or 408, under stringent hybridization conditions. The terms "hybridization" and "stringent conditions" have been described herein above. The corresponding definitions and embodiments apply here mutatis mutandis.

5 The herein disclosed deimmunized CD3 and CD19 binding constructs are particularly useful in the prevention, treatment or amelioration of a proliferative disease, a tumorous disease, an inflammatory disease, an immunological disorder, an autoimmune disease, an infectious disease, a viral disease, allergic reactions, parasitic reactions, graft-versus-host diseases, host-versus-graft diseases or B-cell
10 malignancies, in particular B cell non-Hodgkin's lymphoma, Hodgkin's lymphoma or B cell leukemias (e.g. B cell acute lymphocytic leukemia (B-ALL), (e.g. hairy cell lymphoma) B cell precursor acute lymphatic leukemia (pre-B-ALL), B cell chronic lymphatic leukemia (B-CLL)) leukemia.

15 In a further embodiment, the present invention relates to a CD3 specific binding construct as defined above comprising a first domain specifically binding to human CD3 and having reduced propensity to generate T cell epitopes and a second domain, wherein said second domain is Ig-derived and comprises an antigen-interaction site with a specificity for CD20.

20

CD20 is one of the cell surface proteins present on B-lymphocytes. CD20 antigen is found in normal and malignant pre-B and mature B lymphocytes, including those in over 90% of B-cell non-Hodgkin's lymphomas (NHL). The antigen is absent in hematopoietic stem cells, activated B lymphocytes (plasma cells) and normal tissue.

25 Several antibodies mostly of murine origin have been described: 1F5 (Press et al., 1987, Blood 69/2, 584-591), 2B8 / C2B8, 2H7, 1H4 (Liu et al., 1987, J Immunol 139, 3521-3526; Anderson et al., 1998, US patent No. 5,736,137; Haisma et al., 1998, Blood 92, 184-190; Shan et al., 1999, J. Immunol 162, 6589-6595).

30 CD20 has been described in immunotherapeutic strategies for the treatment of plasma cell malignancies using vaccination with DNA encoding scFv linked to carrier protein (Treon et al., 2000, Semin Oncol 27(5), 598) and in immunotherapeutic treatment using CD20 antibodies (IDEC-C2B8) have been shown to be effective in the treatment of non-Hodgkin's B-cell lymphoma. CD20 antibodies have proven

efficacy and tolerability in non-Hodgkin's lymphoma, achieving response rates of 73% and 48% in previously untreated or relapsed/refractory indolent non-Hodgkin's lymphoma, respectively (Montserrat, 2003, Semin Oncol 30(1suppl2), 34-39). Furthermore, CD20 antibodies have been widely used to treat relapsing or advanced stage B-cell neoplasms with an efficacy of about 50%.

In a particularly preferred embodiment of the present invention, CD3-specific binding constructs are provided, which comprise a deimmunized domain directed against/binding to/interacting with human CD3 and a second Ig-derived domain which specifically binds to/interacts with CD20. Such constructs are shown in Table 8A and 8B. The modules A-G in Tables 8A and 8B can be defined as mentioned above for Tables 1-5. Deimmunized VH domains of antibodies having specificity for the human CD3 antigen can be selected from the sequences as set out in SEQ ID NOs: 74 or 76. Deimmunized VL domains of antibodies having specificity for the human CD3 antigen can be selected from the sequences as set out in SEQ ID NOs: 78, 80 or 82. The VH protein domain of human CD20 antibody is as set out in SEQ ID NO: 170. The VL protein domain of human CD20 antibody is as set out in SEQ ID NO: 172. When either the module pair A/C or E/G is a pair of deimmunized VH/VL or VL/VH protein domains from an antibody having specificity for the human CD3 antigen, protein module B or F, respectively, has the amino acid sequence as set out in SEQ ID NO: 3. When either the module pair A/C or E/G is a pair of VH/VL or VL/VH from an antibody having specificity for the CD20 antigen, protein module B or F, respectively, has the amino acid sequence as set out in SEQ ID NO: 168. The respective groups of protein modules A-B-C and E-F-G are connected to each other through protein module D, having the sequence as set out in SEQ ID NO: 174. However, as mentioned above an additional serine may be introduced for cloning purposes (linker as depicted in SEQ ID NO.:176) between the VL and subsequent V domain.

Nucleic acid molecules encoding deimmunized VH domains of antibodies having specificity for the human CD3 antigen can be selected from the sequences as set out in SEQ ID NOs: 73 or 75. Nucleic acid molecules encoding deimmunized VL domains of antibodies having specificity for the human CD3 antigen can be selected from the sequences as set out in SEQ ID NOs: 77, 79 or 81. The nucleic acid

molecule encoding the VH protein domain of the human CD20 antibody is as set out in SEQ ID NO: 169. The nucleic acid molecule encoding the VL protein domain of the human CD20 antibody is as set out in SEQ ID NO: 171. When either the module pair A/C or E/G denotes a nucleic acid encoding a pair of deimmunized VH/VL or VL/VH protein domains from an antibody having specificity for the human CD3 antigen, nucleic acid module B or F, respectively, has the amino acid sequence as set out in SEQ ID NO: 202. When either the module pair A/C or E/G denotes a nucleic acid encoding a pair of VH/VL or VL/VH from an antibody having specificity for the CD20 antigen, nucleic acid module B or F, respectively, has the nucleic acid sequence as set out in SEQ ID NO: 201. The groups of nucleic acid modules A-B-C and E-F-G are connected to each other through nucleic acid module D, having the sequence as set out in SEQ ID NO: 173. An alternative linker SEQ ID NO.:175 may also be used to conjugate VL domain with a subsequent V domain (including an additional codon encoding a serine residue for cloning purposes).

Table 8A Deimmunized anti-human CD3 constructs comprising single chain anti-CD20 variable regions: amino acid sequence

Construct	SEQ ID NO in construct portion ...							deimmunized anti-CD3 construct / Specificity (N -> C)	Domain Arrangement
	A	B	C	D	E	F	G		
1	80	3	74	174	170	168	172	CD3 (VL2/ VH5) xCD20	LHHL
2	74	3	80	174	170	168	172	CD3 (VH5/VL2) xCD20	HLHL
3	80	3	74	174	172	168	170	CD3 (VL2/ VH5) xCD20	LHLH
4	74	3	80	174	172	168	170	CD3 (VH5/VL2) xCD20	HLLH
5	172	168	170	174	74	3	80	CD20xCD3 (VH5/VL2)	LHHL
6	170	168	172	174	74	3	80	CD20xCD3(VH5/VL2)	HLHL
7	172	168	170	174	80	3	74	CD20xCD3 (VL2/ VH5)	LHLH
8	170	168	172	174	80	3	74	CD20xCD3(VL2/ VH5)	HLLH
9	80	3	76	174	170	168	172	CD3 (VL2/ VH7) xCD20	LHHL
10	76	3	80	174	170	168	172	CD3 (VH7/VL2) xCD20	HLHL
11	80	3	76	174	172	168	170	CD3 (VL2/ VH7) xCD20	LHLH
12	76	3	80	174	172	168	170	CD3 (VH7/VL2) xCD20	HLLH
13	172	168	170	174	76	3	80	CD20xCD3 (VH7/VL2)	LHHL
14	170	168	172	174	76	3	80	CD20xCD3(VH7/VL2)	HLHL
15	172	168	170	174	80	3	76	CD20xCD3 (VL2/ VH7)	LHLH
16	170	168	172	174	80	3	76	CD20xCD3(VL2/ VH7)	HLLH

Table 8B Deimmunized anti-human CD3 constructs comprising single chain anti-CD20 variable regions: Nucleotide sequence

Construct	SEQ ID NO in construct portion ...							deimmunized anti-CD3 construct / Specificity (N -> C)	Domain Arrangement
	A	B	C	D	E	F	G		
1	79	202	73	173	169	201	171	CD3 (VL2/ VH5) xCD20	LHHL
2	73	202	79	173	169	201	171	CD3 (VH5/VL2) xCD20	HLHL
3	79	202	73	173	171	201	169	CD3 (VL2/ VH5) xCD20	LHLH
4	73	202	79	173	171	201	169	CD3 (VH5/VL2) xCD20	HLLH
5	171	201	169	173	73	202	79	CD20xCD3 (VH5/VL2)	LHHL
6	169	201	171	173	73	202	79	CD20xCD3(VH5/VL2)	HLHL
7	171	201	169	173	79	202	73	CD20xCD3 (VL2/ VH5)	LHLH
8	169	201	171	173	79	202	73	CD20xCD3(VL2/ VH5)	HLLH
9	79	202	75	173	169	201	171	CD3 (VL2/ VH7) xCD20	LHHL
10	75	202	79	173	169	201	171	CD3 (VH7/VL2) xCD20	HLHL
11	79	202	75	173	171	201	169	CD3 (VL2/ VH7) xCD20	LHLH
12	75	202	79	173	171	201	169	CD3 (VH7/VL2) xCD20	HLLH
13	171	201	169	173	75	202	79	CD20xCD3 (VH7/VL2)	LHHL
14	169	201	171	173	75	202	79	CD20xCD3(VH7/VL2)	HLHL
15	171	201	169	173	79	202	75	CD20xCD3 (VL2/ VH7)	LHLH
16	169	201	171	173	79	202	75	CD20xCD3(VL2/ VH7)	HLLH

More preferably, the deimmunized CD3 and CD20 binding constructs of the present invention comprises an amino acid sequence which is selected from the group consisting of

- 5 (a) an amino acid sequence as shown in any one of SEQ ID NO 218, 220, 222, 224, 226, or 228 ;
- (b) an amino acid sequence encoded by a nucleic acid sequence as shown in any one of in SEQ ID NO 217, 219, 221, 223, 225 or 227; and
- (c) an amino acid sequence encoded by a nucleic acid sequence which is degenerate as a result of the genetic code to a nucleotide sequence of (b) ;
- 10 (d) and amino acid sequence encoded by a nucleic acid sequence hybridising with the complementary strand of a nucleic acid sequence as defined in (b) under stringent hybridisation conditions.

15 The present invention also provides for CD3 specific binding constructs comprising a first domain which specifically binds to human CD3 and has reduced propensity to generate T cell epitopes and comprising an Ig-derived second domain directed against/ capable of binding to CD20, which comprise an amino acid sequence encoded by a nucleic acid sequence hybridizing with the complementary strand of a nucleic acid sequence as defined in (b) herein above, i.e. to a nucleic acid sequence
20 as shown in any one of SEQ ID NO 217, 219, 221, 223, 225 or 227, under stringent hybridization conditions. The terms "hybridization" and "stringent conditions" have been described herein above. The corresponding definitions and embodiments apply here mutatis mutandis.

25 The herein described deimmunized CD3 and CD20 binding constructs are envisaged for use in the treatment, prevention and/or amelioration of B-cell related disorders, preferably in the medical intervention of lymphoma, more preferably in the treatment of non-Hodgkin lymphoma.

30 The invention also provides for nucleic acid sequence encoding a CD3 specific binding molecule of the invention.

It is evident to the person skilled in the art that regulatory sequences may be added to the nucleic acid molecule of the invention. For example, promoters, transcriptional

enhancers and/or sequences which allow for induced expression of the polynucleotide of the invention may be employed. A suitable inducible system is for example tetracycline-regulated gene expression as described, e.g., by Gossen and Bujard (Proc. Natl. Acad. Sci. USA 89 (1992), 5547-5551) and Gossen et al. (Trends Biotech. 12 (1994), 58-62), or a dexamethasone-inducible gene expression system as described, e.g. by Crook (1989) EMBO J. 8, 513-519 .

Furthermore, it is envisaged for further purposes that nucleic acid molecules may contain, for example, thioester bonds and/or nucleotide analogues. Said modifications may be useful for the stabilization of the nucleic acid molecule against endo- and/or exonucleases in the cell. Said nucleic acid molecules may be transcribed by an appropriate vector containing a chimeric gene which allows for the transcription of said nucleic acid molecule in the cell. In this respect, it is also to be understood that such polynucleotide can be used for "gene targeting" or "gene therapeutic" approaches. In another embodiment said nucleic acid molecules are labeled. Methods for the detection of nucleic acids are well known in the art, e.g., Southern and Northern blotting, PCR or primer extension. This embodiment may be useful for screening methods for verifying successful introduction of the nucleic acid molecules described above during gene therapy approaches.

Said nucleic acid molecule(s) may be a recombinantly produced chimeric nucleic acid molecule comprising any of the aforementioned nucleic acid molecules either alone or in combination. Preferably, the nucleic acid molecule is part of a vector.

The present invention therefore also relates to a vector comprising the nucleic acid molecule described in the present invention.

Many suitable vectors are known to those skilled in molecular biology, the choice of which would depend on the function desired and include plasmids, cosmids, viruses, bacteriophages and other vectors used conventionally in genetic engineering. Methods which are well known to those skilled in the art can be used to construct various plasmids and vectors; see, for example, the techniques described in Sambrook et al. (loc cit.) and Ausubel, Current Protocols in Molecular Biology, Green Publishing Associates and Wiley Interscience, N.Y. (1989), (1994). Alternatively, the polynucleotides and vectors of the invention can be reconstituted into liposomes for

delivery to target cells. As discussed in further details below, a cloning vector was used to isolate individual sequences of DNA. Relevant sequences can be transferred into expression vectors where expression of a particular polypeptide is required. Typical cloning vectors include pBluescript SK, pGEM, pUC9, pBR322 and pGBT9.

5 Typical expression vectors include pTRE, pCAL-n-EK, pESP-1, pOP13CAT.

Preferably said vector comprises a nucleic acid sequence which is a regulatory sequence operably linked to said nucleic acid sequence encoding a bispecific single chain antibody constructs defined herein.

10 Such regulatory sequences (control elements) are known to the artisan and may include a promoter, a splice cassette, translation initiation codon, translation and insertion site for introducing an insert into the vector. Preferably, said nucleic acid molecule is operatively linked to said expression control sequences allowing expression in eukaryotic or prokaryotic cells.

15 It is envisaged that said vector is an expression vector comprising the nucleic acid molecule encoding a bispecific single chain antibody constructs defined herein.

The term "regulatory sequence" refers to DNA sequences, which are necessary to effect the expression of coding sequences to which they are ligated. The nature of such control sequences differs depending upon the host organism. In prokaryotes, control sequences generally include promoter, ribosomal binding site, and 20 terminators. In eukaryotes generally control sequences include promoters, terminators and, in some instances, enhancers, transactivators or transcription factors. The term "control sequence" is intended to include, at a minimum, all components the presence of which are necessary for expression, and may also include additional advantageous components.

25 The term "operably linked" refers to a juxtaposition wherein the components so described are in a relationship permitting them to function in their intended manner. A control sequence "operably linked" to a coding sequence is ligated in such a way that expression of the coding sequence is achieved under conditions compatible with the control sequences. In case the control sequence is a promoter, it is obvious for a 30 skilled person that double-stranded nucleic acid is preferably used.

Thus, the recited vector is preferably an expression vector. An "expression vector" is a construct that can be used to transform a selected host and provides for expression of a coding sequence in the selected host. Expression vectors can for instance be cloning vectors, binary vectors or integrating vectors. Expression comprises

transcription of the nucleic acid molecule preferably into a translatable mRNA. Regulatory elements ensuring expression in prokaryotes and/or eukaryotic cells are well known to those skilled in the art. In the case of eukaryotic cells they comprise normally promoters ensuring initiation of transcription and optionally poly-A signals
 5 ensuring termination of transcription and stabilization of the transcript. Possible regulatory elements permitting expression in prokaryotic host cells comprise, e.g., the P_L , *lac*, *trp* or *tac* promoter in *E. coli*, and examples of regulatory elements permitting expression in eukaryotic host cells are the *AOX1* or *GAL1* promoter in yeast or the CMV-, SV40-, RSV-promoter (Rous sarcoma virus), CMV-enhancer, SV40-enhancer
 10 or a globin intron in mammalian and other animal cells.

Beside elements which are responsible for the initiation of transcription such regulatory elements may also comprise transcription termination signals, such as the SV40-poly-A site or the tk-poly-A site, downstream of the polynucleotide. Furthermore, depending on the expression system used leader sequences capable
 15 of directing the polypeptide to a cellular compartment or secreting it into the medium may be added to the coding sequence of the recited nucleic acid sequence and are well known in the art; see also, e.g., appended example 1. The leader sequence(s) is (are) assembled in appropriate phase with translation, initiation and termination sequences, and preferably, a leader sequence capable of directing secretion of
 20 translated protein, or a portion thereof, into the periplasmic space or extracellular medium. Optionally, the heterologous sequence can encode a fusion protein including an N-terminal identification peptide imparting desired characteristics, e.g., stabilization or simplified purification of expressed recombinant product; see supra. In this context, suitable expression vectors are known in the art such as Okayama-Berg
 25 cDNA expression vector pcDV1 (Pharmacia), pCDM8, pRc/CMV, pcDNA1, pcDNA3 (In-vitro-gene), pEF-DHFR, pEF-ADA or pEF-neo (Raum et al. Cancer Immunol Immunother (2001) 50(3), 141-150) or pSPORT1 (GIBCO BRL).

Preferably, the expression control sequences will be eukaryotic promoter systems in
 30 vectors capable of transforming or transfecting eukaryotic host cells, but control sequences for prokaryotic hosts may also be used. Once the vector has been incorporated into the appropriate host, the host is maintained under conditions suitable for high level expression of the nucleotide sequences, and as desired, the collection and purification of the polypeptide of the invention may follow; see, e.g.,

the appended examples.

An alternative expression system which could be used to express a cell cycle interacting protein is an insect system. In one such system, *Autographa californica* nuclear polyhedrosis virus (AcNPV) is used as a vector to express foreign genes in *Spodoptera frugiperda* cells or in *Trichoplusia* larvae. The coding sequence of a recited nucleic acid molecule may be cloned into a nonessential region of the virus, such as the polyhedrin gene, and placed under control of the polyhedrin promoter. Successful insertion of said coding sequence will render the polyhedrin gene inactive and produce recombinant virus lacking coat protein coat. The recombinant viruses are then used to infect *S. frugiperda* cells or *Trichoplusia* larvae in which the protein of the invention is expressed (Smith, J. Virol. 46 (1983), 584; Engelhard, Proc. Nat. Acad. Sci. USA 91 (1994), 3224-3227).

Additional regulatory elements may include transcriptional as well as translational enhancers. Advantageously, the above-described vectors of the invention comprises a selectable and/or scorable marker.

Selectable marker genes useful for the selection of transformed cells and, e.g., plant tissue and plants are well known to those skilled in the art and comprise, for example, antimetabolite resistance as the basis of selection for dhfr, which confers resistance to methotrexate (Reiss, Plant Physiol. (Life Sci. Adv.) 13 (1994), 143-149); npt, which confers resistance to the aminoglycosides neomycin, kanamycin and paromycin (Herrera-Estrella, EMBO J. 2 (1983), 987-995) and hygromycin (Marsh, Gene 32 (1984), 481-485). Additional selectable genes have been described, namely trpB, which allows cells to utilize indole in place of tryptophan; hisD, which allows cells to utilize histinol in place of histidine (Hartman, Proc. Natl. Acad. Sci. USA 85 (1988), 8047); mannose-6-phosphate isomerase which allows cells to utilize mannose (WO 94/20627) and ODC (ornithine decarboxylase) which confers resistance to the ornithine decarboxylase inhibitor, 2-(difluoromethyl)-DL-ornithine, DFMO (McConlogue, 1987, In: Current Communications in Molecular Biology, Cold Spring Harbor Laboratory ed.) or deaminase from *Aspergillus terreus* which confers resistance to Blasticidin S (Tamura, Biosci. Biotechnol. Biochem. 59 (1995), 2336-2338).

Useful scorable markers are also known to those skilled in the art and are commercially available. Advantageously, said marker is a gene encoding luciferase (Giacomin, Pl. Sci. 116 (1996), 59-72; Scikantha, J. Bact. 178 (1996), 121), green

fluorescent protein (Gerdes, FEBS Lett. 389 (1996), 44-47) or β -glucuronidase (Jefferson, EMBO J. 6 (1987), 3901-3907). This embodiment is particularly useful for simple and rapid screening of cells, tissues and organisms containing a recited vector.

- 5 As described above, the recited nucleic acid molecule can be used alone or as part of a vector to express the encoded CD3 specific construct in cells, for, e.g., purification but also for gene therapy purposes. The nucleic acid molecules or vectors containing the DNA sequence(s) encoding any one of the above described (bispecific) CD3 constructs is introduced into the cells which in turn produce the
- 10 polypeptide of interest. Gene therapy, which is based on introducing therapeutic genes into cells by ex-vivo or in-vivo techniques is one of the most important applications of gene transfer. Suitable vectors, methods or gene-delivery systems for in-vitro or in-vivo gene therapy are described in the literature and are known to the person skilled in the art; see, e.g., Giordano, Nature Medicine 2 (1996), 534-539;
- 15 Schaper, Circ. Res. 79 (1996), 911-919; Anderson, Science 256 (1992), 808-813; Verma, Nature 389 (1994), 239; Isner, Lancet 348 (1996), 370-374; Muhlhauser, Circ. Res. 77 (1995), 1077-1086; Onodera, Blood 91 (1998), 30-36; Verma, Gene Ther. 5 (1998), 692-699; Nabel, Ann. N.Y. Acad. Sci. 811 (1997), 289-292; Verzeletti, Hum. Gene Ther. 9 (1998), 2243-51; Wang, Nature Medicine 2 (1996), 714-716; WO
- 20 94/29469; WO 97/00957, US 5,580,859; US 5,589,466; or Schaper, Current Opinion in Biotechnology 7 (1996), 635-640. The recited nucleic acid molecules and vectors may be designed for direct introduction or for introduction via liposomes, or viral vectors (e.g., adenoviral, retroviral) into the cell. Preferably, said cell is a germ line cell, embryonic cell, or egg cell or derived therefrom, most preferably said cell is a
- 25 stem cell. An example for an embryonic stem cell can be, inter alia, a stem cell as described in, Nagy, Proc. Natl. Acad. Sci. USA 90 (1993), 8424-8428.

In accordance with the above, the present invention relates to methods to derive vectors, particularly plasmids, cosmids, viruses and bacteriophages used

30 conventionally in genetic engineering that comprise a nucleic acid molecule encoding the polypeptide sequence of a bispecific single chain antibody constructs defined herein. Preferably, said vector is an expression vector and/or a gene transfer or targeting vector. Expression vectors derived from viruses such as retroviruses, vaccinia virus, adeno-associated virus, herpes viruses, or bovine papilloma virus,

may be used for delivery of the recited polynucleotides or vector into targeted cell populations. Methods which are well known to those skilled in the art can be used to construct recombinant vectors; see, for example, the techniques described in Sambrook et al. (loc cit.), Ausubel (1989, loc cit.) or other standard text books.

5 Alternatively, the recited nucleic acid molecules and vectors can be reconstituted into liposomes for delivery to target cells. The vectors containing the nucleic acid molecules of the invention can be transferred into the host cell by well-known methods, which vary depending on the type of cellular host. For example, calcium chloride transfection is commonly utilized for prokaryotic cells, whereas calcium
10 phosphate treatment or electroporation may be used for other cellular hosts; see Sambrook, supra.

The recited vector may, inter alia, be the pEF-DHFR, pEF-ADA or pEF-neo. The vectors pEF-DHFR, pEF-ADA and pEF-neo have been described in the art, e.g. in Mack et al. (PNAS (1995) 92, 7021-7025) and Raum et al. (Cancer Immunol
15 Immunother (2001) 50(3), 141-150).

The invention also provides for a host transformed or transfected with a vector as described herein. Said host may be produced by introducing said at least one of the above described vector or at least one of the above described nucleic acid molecules
20 into the host. The presence of said at least one vector or at least one nucleic acid molecule in the host may mediate the expression of a gene encoding the above described bispecific single chain antibody constructs.

The described nucleic acid molecule or vector which is introduced in the host may either integrate into the genome of the host or it may be maintained
25 extrachromosomally.

The host can be any prokaryote or eukaryotic cell.

The term "prokaryote" is meant to include all bacteria which can be transformed or transfected with DNA or RNA molecules for the expression of a protein of the invention. Prokaryotic hosts may include gram negative as well as gram positive
30 bacteria such as, for example, *E. coli*, *S. typhimurium*, *Serratia marcescens* and *Bacillus subtilis*. The term "eukaryotic" is meant to include yeast, higher plant, insect and preferably mammalian cells. Depending upon the host employed in a recombinant production procedure, the protein encoded by the polynucleotide of the present invention may be glycosylated or may be non-glycosylated. Especially

preferred is the use of a plasmid or a virus containing the coding sequence of the polypeptide of the invention and genetically fused thereto an N-terminal FLAG-tag and/or C-terminal His-tag. Preferably, the length of said FLAG-tag is about 4 to 8 amino acids, most preferably 8 amino acids. An above described polynucleotide can be used to transform or transfect the host using any of the techniques commonly known to those of ordinary skill in the art. Furthermore, methods for preparing fused, operably linked genes and expressing them in, e.g., mammalian cells and bacteria are well-known in the art (Sambrook, loc cit.).

Preferably, said the host is a bacteria, an insect, fungal, plant or animal cell.

It is particularly envisaged that the recited host may be a mammalian cell, more preferably a human cell or human cell line.

Particularly preferred host cells comprise CHO cells, COS cells, myeloma cell lines like SP2/0 or NS/0. As illustrated in the appended examples, particularly preferred are CHO-cells as hosts.

In a further embodiment, the present invention thus relates to a process for the preparation of a CD3 specific construct described above comprising cultivating a cell and/or the host of the invention under conditions suitable for the expression of said construct and isolating the construct from the cell or the culture medium.

The transformed hosts can be grown in fermentors and cultured according to techniques known in the art to achieve optimal cell growth. The polypeptide of the invention can then be isolated from the growth medium, cellular lysates, or cellular membrane fractions. The isolation and purification of the, e.g., microbially expressed polypeptides of the invention may be by any conventional means such as, for example, preparative chromatographic separations and immunological separations such as those involving the use of monoclonal or polyclonal antibodies directed, e.g., against a tag of the polypeptide of the invention or as described in the appended examples.

Furthermore, the invention provides for a composition comprising a (human) CD3-specific binding construct as defined herein or a (human) CD3-specific binding construct as produced by the process disclosed above, a nucleic acid molecule of the invention, a vector or a host of the invention. Said composition may, optionally, also comprise a proteinaceous compound capable of providing an activation signal for

immune effector cells. Most preferably, said composition is a pharmaceutical composition further comprising, optionally, suitable formulations of carrier, stabilizers and/or excipients.

- 5 In accordance with this invention, the term "pharmaceutical composition" relates to a composition for administration to a patient, preferably a human patient. In a preferred embodiment, the pharmaceutical composition comprises a composition for parenteral, transdermal, intraluminal, intra arterial, intrathecal administration or by direct injection into the tissue or tumour. It is in particular envisaged that said
- 10 pharmaceutical composition is administered to a patient via infusion or injection. Administration of the suitable compositions may be effected by different ways, e.g., by intravenous, intraperitoneal, subcutaneous, intramuscular, topical or intradermal administration. The pharmaceutical composition of the present invention may further comprise a pharmaceutically acceptable carrier. Examples of suitable pharmaceutical
- 15 carriers are well known in the art and include phosphate buffered saline solutions, water, emulsions, such as oil/water emulsions, various types of wetting agents, sterile solutions, etc. Compositions comprising such carriers can be formulated by well known conventional methods. These pharmaceutical compositions can be administered to the subject at a suitable dose. The dosage regimen will be
- 20 determined by the attending physician and clinical factors. As is well known in the medical arts, dosages for any one patient depends upon many factors, including the patient's size, body surface area, age, the particular compound to be administered, sex, time and route of administration, general health, and other drugs being administered concurrently. Generally, the regimen as a regular administration of the
- 25 pharmaceutical composition should be in the range of 1 μg to 5 g units per day. However, a more preferred dosage for continuous infusion might be in the range of 0.01 μg to 2 mg, preferably 0.01 μg to 1 mg, more preferably 0.01 μg to 100 μg , even more preferably 0.01 μg to 50 μg and most preferably 0.01 μg to 10 μg units per kilogram of body weight per hour. Particularly preferred dosages are recited herein
- 30 below. Progress can be monitored by periodic assessment. Dosages will vary but a preferred dosage for intravenous administration of DNA is from approximately 10^6 to 10^{12} copies of the DNA molecule. The compositions of the invention may be administered locally or systematically. Administration will generally be parenterally, e.g., intravenously; DNA may also be administered directed to the target site, e.g., by

biolistic delivery to an internal or external target site or by catheter to a site in an artery. Preparations for parenteral administration include sterile aqueous or non-aqueous solutions, suspensions, and emulsions. Examples of non-aqueous solvents are propylene glycol, polyethylene glycol, vegetable oils such as olive oil, and injectable organic esters such as ethyl oleate. Aqueous carriers include water, alcoholic/aqueous solutions, emulsions or suspensions, including saline and buffered media. Parenteral vehicles include sodium chloride solution, Ringer's dextrose, dextrose and sodium chloride, lactated Ringer's, or fixed oils. Intravenous vehicles include fluid and nutrient replenishes, electrolyte replenishers (such as those based on Ringer's dextrose), and the like. Preservatives and other additives may also be present such as, for example, antimicrobials, anti-oxidants, chelating agents, and inert gases and the like. In addition, the pharmaceutical composition of the present invention might comprise proteinaceous carriers, like, e.g., serum albumine or immunoglobuline, preferably of human origin. It is envisaged that the pharmaceutical composition of the invention might comprise, in addition to the proteinaceous bispecific single chain antibody constructs or nucleic acid molecules or vectors encoding the same (as described in this invention), further biologically active agents, depending on the intended use of the pharmaceutical composition. Such agents might be drugs acting on the gastro-intestinal system, drugs acting as cytostatica, drugs preventing hyperurikemia, drugs inhibiting immunereactions (e.g. corticosteroids), drugs acting on the circulatory system and/or agents such as T-cell co-stimulatory molecules or cytokines known in the art.

Possible indications for administration of the composition(s) of the invention are tumorous diseases especially epithelial cancers/carcinomas such as breast cancer, colon cancer, prostate cancer, head and neck cancer, skin cancer (melanoma), cancers of the genito-urinary tract, e.g. ovarian cancer, endometrial cancer, cervix cancer and kidney cancer, lung cancer, gastric cancer, cancer of the small intestine, liver cancer, pancreas cancer, gall bladder cancer, cancers of the bile duct, esophagus cancer, cancer of the salivatory glands and cancer of the thyroid gland or other tumorous diseases like haematological tumors, gliomas, sarcomas or osteosarcomas. The administration of the composition(s) of the invention is especially indicated for minimal residual disease, preferably early solid tumors, advanced solid tumors or metatatic solid tumors, which is characterized by the local and non-local reoccurrence of the tumor caused by the survival of single cells.

The invention further envisages the co-administration protocols with other compounds, e.g. molecules capable of providing an activation signal for immune effector cells, for cell proliferation or for cell stimulation. Said molecule may be, e.g. a further primary activation signal for T cells (e.g. a further costimulatory molecule: molecules of B7 family, Ox40L, 4.1 BBL), or a further cytokine: interleukin (e.g. IL-2) or NKG-2D engaging compound.

The composition of the invention as described above may also be a diagnostic composition further comprising, optionally, means and methods for detection.

10

The CD3-specific constructs provided herein are also suited for use in immunoassays in which they can be utilized in liquid phase or bound to a solid phase carrier. Examples of immunoassays which can utilize the polypeptide of the invention are competitive and non-competitive immunoassays in either a direct or indirect format. Examples of such immunoassays are the enzyme linked immunosorbent assay (ELISA), enzyme immunoassay (EIA), radioimmunoassay (RIA), the sandwich (immunometric assay) and the Western blot assay.

The CD3 specific binding constructs of the invention can be bound to many different carriers and used to isolate cells specifically bound to said polypeptides. Examples of well-known carriers include glass, polystyrene, polyvinyl chloride, polypropylene, polyethylene, polycarbonate, dextran, nylon, amyloses, natural and modified celluloses, polyacrylamides, agaroses, and magnetite. The nature of the carrier can be either soluble or insoluble, e.g. as beads, for the purposes of the invention.

There are many different labels and methods of labeling known to those of ordinary skill in the art. Examples of the types of labels which can be used in the present invention include enzymes, radioisotopes, colloidal metals, fluorescent compounds, chemiluminescent compounds, and bioluminescent compounds; see also the embodiments discussed hereinabove.

30

In a most preferred embodiment of the present invention, the use of a CD3 specific binding molecule of the invention, of a vector or of a host of the invention for the preparation of a pharmaceutical composition is envisaged. Said pharmaceutical composition may be employed in the prevention, treatment or amelioration of a

proliferative disease, a tumorous disease, an inflammatory disease, an immunological disorder, an autoimmune disease, an infectious disease, viral disease, allergic reactions, parasitic reactions, graft-versus-host diseases or host-versus-graft diseases.

5

Furthermore, in accordance to the invention, the deimmunized constructs comprising CD19 and CD3 binding domains, preferably SEQ ID NO.190, 192, 194, 196, 198, 200, 327, 329, 331, 333, 335, 337, 339, 341, 343, 345, 347, 349, 351, 353, 357, 359, 361, 363, 365, 367, 369, 371, 373, 375, 377, 379, 381, 383, 385, 387, 389, 391, 393, 395, 397, 399, 401, 403, 405, 407 or 409, can be used for the treatment of immunological disorders (various B cell malignancies) or autoimmune diseases, the deimmunized constructs comprising CCR5 and CD3 binding domains, preferably SEQ ID NO.206, 208, 210, 212, 214 or 216, can be used for the treatment of viral diseases (HIV), autoimmune diseases and/or of inflammatory diseases (like rheumatoid arthritis), the deimmunized constructs comprising CD20 and CD3 binding domains, preferably SEQ ID NO.218, 220, 222, 224, 226, 228, can be used for the treatment of tumorous diseases, preferably lymphoma, more preferably non-Hodgkin's B-cell lymphoma and the deimmunized constructs comprising EpCAM and CD3 binding domains, preferably SEQ ID NO.31, 33, 35, 37, 39, 49, 55, 58, 61, 63, 65, 67, 237, 239, 241, 243, 245, 247, 249, 251, 253, 255, 257, 259, 261, 263, 265, 267, 269, 271, 273, 275, 277, 279, 281, 283, 285, 287, 289, 291, 293, 295, 297, 299, 301, 303, 305, 307, 309, 311, 313, 315, 317, 319, 321, 323 or 325 can be used for the treatment of tumorous diseases, preferably epithelial cancers.

25

The invention also relates to a method for the prevention, treatment or amelioration of a proliferative disease, a tumorous disease, an inflammatory disease, an immunological disorder, an autoimmune disease, an infectious disease, viral disease, allergic reactions, parasitic reactions, graft-versus-host diseases or host-versus-graft diseases comprising the administration of a (bispecific) CD3 specific binding molecule of the invention or a (bispecific) CD3 specific binding molecule as produced by the process described herein, of a nucleic acid molecule, a vector or a host of the invention to a subject in need of such a prevention, treatment or amelioration . Preferably, said subject is a human.

30

The method for the prevention, treatment or amelioration may also, in addition, comprise the administration of a proteinaceous compound capable of providing an activation signal for immune effector cells. Said proteinaceous compound may be administered simultaneously or non-simultaneously with the CD3 binding molecule, a nucleic acid molecule, a vector or a host of the invention. The proteinaceous compound may, inter alia, selected from the group consisting of a further costimulatory molecule: molecules of B7 family, Ox40L, 4.1 BBL), or a further cytokine: interleukin (e.g. IL-2) or NKG-2D engaging compounds.

Finally, the invention provides for a kit comprising the CD3 specific binding molecule, a nucleic acid molecule, a vector or a host of the invention.

Said kit is particularly useful in the preparation of the pharmaceutical composition of the present invention and may, inter alia, consist of a container useful for injections or infusions. Advantageously, the kit of the present invention further comprises, optionally (a) buffer(s), storage solutions and/or remaining reagents or materials required for the conduct of medical or scientific purposes. Furthermore, parts of the kit of the invention can be packaged individually in vials or bottles or in combination in containers or multicontainer units. The kit of the present invention may be advantageously used, inter alia, for carrying out the method of the invention and could be employed in a variety of applications referred herein, e.g., as research tools or medical tools. The manufacture of the kits preferably follows standard procedures which are known to the person skilled in the art.

These and other embodiments are disclosed and encompassed by the description and Examples of the present invention. Further literature concerning any one of the antibodies, methods, uses and compounds to be employed in accordance with the present invention may be retrieved from public libraries and databases, using for example electronic devices. For example, the public database "Medline", available on the Internet, may be utilized, for example under <http://www.ncbi.nlm.nih.gov/PubMed/medline.html>. Further databases and addresses, such as <http://www.ncbi.nlm.nih.gov/>, <http://www.infobiogen.fr/>, http://www.fmi.ch/biology/research_tools.html, <http://www.tigr.org/>, are known to the person skilled in the art and can also be obtained using, e.g., <http://www.lycos.com>.

The figures show:

Figure 1. DNA and amino acid sequences of non-deimmunized anti-CD3 cassette (SEQ ID Nos 1 and 2).

5

Figure 2. A) Amino acid sequences of the heavy chains VH2 (SEQ ID NO.:70), VH3 (SEQ ID NO.:72), VH5 (SEQ ID NO.:74) and VH7 (SEQ ID NO.:76) and light chains VL1 (SEQ ID NO.:78), VL2 (SEQ ID NO.:80) and VL3 (SEQ ID NO.:82), respectively,

10 B) Nucleotide sequences of the heavy chains VH2 (SEQ ID NO.:69), VH3 (SEQ ID NO.:71), VH5 (SEQ ID NO.:73) and VH7 (SEQ ID NO.:75) and light chains VL1 (SEQ ID NO.:77), VL2 (SEQ ID NO.:79) and VL3 (SEQ ID NO.:81), respectively, C) Amino

acid sequences of the CDRs 1, 2 and 3 of the heavy chains of the non-deimmunized anti-CD3 (SEQ ID NO.:84, 90, 96, respectively), VH2 (SEQ ID NO.:86, 94, 96, respectively), VH3 (SEQ ID NO.:86, 94, 96, respectively), VH5 (SEQ ID NO.:88, 92, 96, respectively) and VH7 (SEQ ID NO.:88, 90, 96, respectively) and of the light

15 chains of the non-deimmunized anti-CD3 (SEQ ID NO.:98, 102, 104, respectively), chains VL1 (SEQ ID NO.:100, 102, 104, respectively), VL2 (SEQ ID NO.:100, 102, 104, respectively) and VL3 (SEQ ID NO.:98, 102, 104, respectively) and D)

20 Nucleotide sequences of the CDRs 1, 2 and 3 of the heavy chains of the non-deimmunized anti-CD3 (SEQ ID NO.:83, 89, 95, respectively), VH2 (SEQ ID NO.:85, 93, 95, respectively), VH3 (SEQ ID NO.:85, 93, 95, respectively), VH5 (SEQ ID NO.:87, 91, 95, respectively) and VH7 (SEQ ID NO.:87, 89, 95, respectively) and of

the light chains of the non-deimmunized anti-CD3 (SEQ ID NO.:97, 101, 103, respectively), chains VL1 (SEQ ID NO.:99, 101, 103, respectively), VL2 (SEQ ID NO.:99, 101, 103, respectively) and VL3 (SEQ ID NO.:97, 101, 103, respectively).

25

Figure 3. A) Nucleotide sequence of anti-CD3 (VH2/VL1) (SEQ ID NO.:4) B) Amino acid sequence of anti-CD3 (VH2/VL1) (SEQ ID NO.:5) C) Nucleotide sequence of anti-CD3 (VH2/VL2) (SEQ ID NO.:6) D) Amino acid sequence of anti-CD3 (VH2/VL2) (SEQ ID NO.:7) E) Nucleotide sequence of anti-CD3 (VH2/VL3) (SEQ ID NO.:8) F) Amino acid sequence of anti-CD3 (VH2/VL3) (SEQ ID NO.:9).

30

Figure 4. A) Nucleotide sequence of anti-CD3 (VH3/VL1) (SEQ ID NO.:10) B) Amino acid sequence of anti-CD3 (VH3/VL1) (SEQ ID NO.:11) C) Nucleotide sequence of

anti-CD3 (VH3/VL2) (SEQ ID NO.:12) D) Amino acid sequence of anti-CD3 (VH3/VL2) (SEQ ID NO.:13) E) Nucleotide sequence of anti-CD3 (VH3/VL3) (SEQ ID NO.:14) F) Amino acid sequence of anti-CD3 (VH3/VL3) (SEQ ID NO.:15).

5 **Figure 5.** A) Nucleotide sequence of anti-CD3 (VH5/VL1) (SEQ ID NO.:16) B) Amino acid sequence of anti-CD3 (VH5/VL1) (SEQ ID NO.:17) C) Nucleotide sequence of anti-CD3 (VH5/VL2) (SEQ ID NO.:18) D) Amino acid sequence of anti-CD3 (VH5xVL2) (SEQ ID NO.:19) E) Nucleotide sequence of anti-CD3 (VH5/VL3) (SEQ ID NO.:20) F) Amino acid sequence of anti-CD3 (VH5/VL3) (SEQ ID NO.:21).

10

Figure 6. A) Nucleotide sequence of anti-CD3 (VH7/VL1) (SEQ ID NO.:22) B) Amino acid sequence of anti-CD3 (VH7xVL1) (SEQ ID NO.:23) C) Nucleotide sequence of anti-CD3 (VH7/VL2) (SEQ ID NO.:24) D) Amino acid sequence of anti-CD3 (VH7xVL2) (SEQ ID NO.:25) E) Nucleotide sequence of anti-CD3 (VH7/VL3) (SEQ ID NO.:26) F) Amino acid sequence of anti-CD3 (VH7/VL3) (SEQ ID NO.:27).

15

Figure 7. Binding of bispecific anti-CD19 constructs with different deimmunized anti-CD3 parts: the anti-CD3 (VH2/VL1) (SEQ ID NO.:178), anti-CD3 (VH2/VL2) (SEQ ID NO.:180), anti-CD3 (VH2/VL3) (SEQ ID NO.:182), anti-CD3 (VH3/VL1) (SEQ ID NO.:184), anti-CD3 (VH3/VL2) (SEQ ID NO.:186), anti-CD3 (VH3/VL3) (SEQ ID NO.:188), anti-CD3 (VH5/VL1) (SEQ ID NO.:190), anti-CD3 (VH5/VL2) (SEQ ID NO.:192), anti-CD3 (VH5/VL3) (SEQ ID NO.:194), anti-CD3 (VH7/VL1) (SEQ ID NO.:196), anti-CD3 (VH7/VL2) (SEQ ID NO.:198), anti-CD3 (VH7/VL3) (SEQ ID NO.:200) A) CD3 and B) CD19. Binding was measured by a FACS-based assay using CD3 enriched PBMCs (A) or CD19-positive NALM-cells (B). CD3 and a secondary FITC labeled anti-mouse Ig antibody was used as a negative control in (A) and CD19 and a secondary FITC labeled anti-mouse Ig antibody was used as a negative control in (B). Constructs anti-CD19xanti-CD3 and anti-EpCAM (M79)xanti-CD3 were used as controls. MFI indicates mean fluorescence intensity.

25
30

Figure 8: A representative elution pattern of a deimmunized variant of anti CD19 x anti CD3 protein fraction from a HCIC column at 280 nm. The bottom line showing a major step at 700 ml indicates the theoretical gradient of the elution buffer containing 20 mM acetate, pH3.5. High adsorption at 280 nm was due to non-bound protein in

the column flow-through. The arrow at 810,98 ml indicates the eluted deimmunized anti-CD3 fraction.

Figure 9: A representative elution pattern of a deimmunized variant of anti CD19 x anti CD3 protein fraction from a Ni-Chelating His Trap® column at 280 nm. The bottom line showing a first step at 85 ml and a second major step at 90 ml indicates the theoretical gradient of the elution buffer (dotted line). The arrow at 93,16 ml indicates the protein fraction containing the antiCD19 x antiCD3 construct.

Figure 10: A representative protein elution pattern from a Sephadex S200 gelfiltration column. Fractions were collected from 0-130 ml retention time. The protein peak at 80.44 ml corresponds to a MW of ca. 52 kD and contains the deimmunized antiCD19 x antiCD3 construct.

Figure 11: A) SDS-PAGE analysis of deimmunized variants of anti CD19 x anti CD3 protein fractions. Lane M: Molecular weight marker Lane 1: HCIC flowthrough; lane 2: cell culture supernatant; lane 3: HCIC eluate; lane 4: IMAC flowthrough; lane 5: IMAC wash; lane 6: IMAC eluate; lane 7: gel filtration eluate; B) Western blot analysis of purified deimmunized variants of anti CD19 x anti CD3 protein fractions. Western blot analysis of purified bispecific protein was performed with antibodies directed against the His-Tag (PentaHis, Qiagen) and goat anti mouse Ig labeled with alkaline phosphatase. Lane M: Molecular weight marker Lane 1: HCIC flow through; lane 2: cell culture supernatant; lane 3: HCIC eluate; lane 4: IMAC flow through; lane 5: IMAC wash; lane 6: IMAC eluate; lane 7: gel filtration eluate.

Figure 12. Binding of the purified bispecific anti-CD19 constructs with different deimmunized anti-CD3 parts anti-CD3 (VH5/VL1) (SEQ ID NO.:190), anti-CD3 (VH7/VL1) (SEQ ID NO.:196), anti-CD3 (VH7/VL2) (SEQ ID NO.:198) and anti-CD3 (VH7/VL3) (SEQ ID NO.:200) to A) CD3 and B) CD19 compared to the wild-type anti CD19xanti CD3 construct. Binding was measured by a FACS-based assay using CD3 enriched PBMCs (A) or CD19-positive NALM-cells (B). A secondary antibody with CD3 positive cells was used as a negative control in (A) and a secondary antibody with CD19 positive cells was used as a negative control in (B). Constructs anti-CD19xanti-CD3 and anti-EpCAM (M79)xanti-CD3 were used as controls. Assay

was carried out with concentrations of 1 µg/ml and 5 µg/ml. MFI indicates mean fluorescence intensity.

Figure 13. Cytotoxicity assay of bispecific anti-CD19 constructs with different deimmunized anti-CD3 parts anti-CD3 (VH5/VL1) (SEQ ID NO.:190), anti-CD3 (VH5/VL2) (SEQ ID NO.:192), anti-CD3 (VH5/VL3) (SEQ ID NO.:194), anti-CD3 (VH7/VL1) (SEQ ID NO.:196), anti-CD3 (VH7/VL2) (SEQ ID NO.:198) and anti-CD3 (VH7/VK3) (SEQ ID NO.:200) compared to control.

Figure 14. Sequence alignment of variable heavy region of the non-deimmunized CD3 antibody, VH5 (SEQ ID NO.:74), VH7 (SEQ ID NO.:76), VH2 (SEQ ID NO.:70) and VH3 (SEQ ID NO.:72). Framework region 1 (FR1), complementarity determining region 1 (CDR1), Framework region 1 (FR1), complementarity determining region 2 (CDR2), Framework region 3 (FR3), complementarity determining region 3 (CDR3) and Framework region 4 (FR4) have been depicted. The sequence LAR and VKK in FR1, the sequence ASGYTF and ASGYTA at the transition of framework 1 region to CDR1 region and the sequence LTTDK, ITTDK and MTTDT at FR3 and the sequence MQLS, MELS and LQMN at FR3 have been boxed. Alignment was carried out using the AlingnX program of Vector NTI Advance (Informax, Inc., USA).

Figure 15. Binding analysis of bispecific anti EpCAM constructs with different deimmunized anti-CD3 parts: anti-CD3 (VH5/VL2)x5-10 (SEQ ID NO.:37) (A), deimmunized anti-CD3 (VH5/VL2)x4-7 (SEQ ID NO.:33), (B) deimmunized anti-CD3 (VH5/VL2)x3-1 (SEQ ID NO.:31) (C), deimmunized anti-CD3 (VH5/VL2)x4-7 (VL-VH) (SEQ ID NO.:35) (D) and deimmunized anti-CD3 (VH5/VL2)x5-10 (VL-VH) (SEQ ID NO.:39) (E) in CD3-positive Jurkat and EpCAM-positive Kato III cells with a FACS-based assay. A shift to the right shows binding. In Jurkat cells the dotted line indicates the shift of the negative control (only secondary antibody), dashed line shows the binding of an anti-EpCAM-anti-CD3 control antibody, the bold line shows the bispecific construct of interest. In the binding assay using EpCAM-positive Kato III-cells instead of monoclonal antibody to CD3 a monoclonal antibody to EpCAM was used as a positive control.

Figure 16. Binding analysis of bispecific anti EpCAM constructs with different deimmunized anti-CD3 parts: 3-1xanti-CD3 (VH5/VL2) (SEQ ID NO.:49) (A) and 5-10xanti-CD3 (VH5/VL2) (SEQ ID NO.:63) (B) in CD3-positive Jurkat cells and in EpCAM-positive Kato cells with a FACS based assay. A shift to the right shows binding.

Figure 17. Cytotoxicity assay of EpCAM constructs with deimmunized anti-CD3 parts (di anti-CD3) at N-terminal position anti-CD3 (VH5/VL2)x3-1 (SEQ ID NO.:31), anti-CD3 (VH5/VL2)x-5-10 (SEQ ID NO.:37) and anti-CD3 (VH5/VL2)x4-7 (SEQ ID NO.:33) compared to the corresponding non-deimmunized constructs. CB15 T cell clone and CHO-EpCAM cells were used in an E:T ratio of 5:1. CHO-EpCAM cell were stained with PKH26 dye and the cells were counted after bispecific single chain antibody incubation with FACS analysis.

Figure 18. Cytotoxicity assay of EpCAM constructs with deimmunized anti-CD3 parts at the C-terminal position 3-1xanti-CD3 (VH5/VL2) (SEQ ID NO.:49) and 5-10xanti-CD3 (VH5/VL2) (SEQ ID NO.:63) compared to the corresponding non-deimmunized wild-type constructs. Cytotoxicity assay was carried out identically to Figure 17.

The following Examples illustrate the invention:

In the following examples a number of single chain anti-human CD3 antibodies have been engineered to show reduced immunogenicity in man. The different deimmunized anti-human CD3 antibodies comprise 12 combinations of 4 different VH (VH2 (SEQ ID NO.:69, 70), VH3 (SEQ ID NO.:71, 72), VH5 (SEQ ID NO.:73, 74) and VH7 (SEQ ID NO.:75, 76)) and 3 different VL (VL1 (SEQ ID NO.:77, 78), VL2 (SEQ ID NO.:79, 80) and VL3 (SEQ ID NO.:81, 82)) regions joined together. The amino acid and nucleic acid sequences of the above-mentioned VH and VL regions are shown in Figures 3-6. Illustratively, the deimmunized anti-CD3 single chain antibodies were combined with an anti-CD19 single chain antibody or with an anti-EpCAM single chain antibody in order to form a bispecific product.

Example 1. Cloning and expression of deimmunized anti-CD3 constructs

1.1. Transfer of cDNA encoding single chain antibody

The DNA encoding the anti-CD3 single-chain antibody, which was deimmunized, is referred herein as the anti-CD3 cassette. This anti-CD3 cassette consists of a
 5 SGGGGS linker (SEQ ID NO.:176), the anti-CD3 VH region (SEQ ID NO.:110), a 14 amino acid GS linker (VEGGSGGSGGSGGSGGVD linker (SEQ ID NO.:68)), and the anti-CD3 VL chains region (SEQ ID NO.:112) followed by 6 histidine residues. The afore-mentioned DNA was cloned into the vector p-PCR-Script-Amp SK(+) (Stratagene) at the Srf1 site. The DNA and amino acid sequence of the anti-CD3
 10 cassette is shown in SEQ ID NO.:1, SEQ ID NO.:2 and Figure 1.

1.2 Computer analysis of sequences for immunogenic T cell epitopes and design of deimmunized single chain antibody sequences

The amino acid sequence of the anti-CD3 cassette (SEQ ID NO.:2) was analyzed by
 15 peptide threading program to identify potential T cell epitopes with the method as described in WO 98/52976. SEQ ID NO.3 shows the deimmunized linker sequence and SEQ ID NO.:68 the original linker sequence.

1.3 Construction of deimmunized single chain antibody sequences

20 The deimmunized versions of the anti-CD3 cassette were constructed by the method of overlapping PCR recombination. The anti-CD3 cassette (SEQ ID NO.:1, 2) in pPCR-S-Amp SK+ was used as the template for mutagenesis to the required deimmunized sequences. Sets of mutagenic primer pairs were synthesized encompassing the regions to be altered. The deimmunized sequences produced,
 25 including 4 different VH and 3 different VL regions, were cloned as Not1 to Hind111 fragments into the vector pPCR-S-Amp SK+ and the entire DNA sequence was confirmed to be correct. The 4 different VH and 3 different VK regions were joined in all combinations (a total of 12), either by PCR or using a unique BstE11 site introduced at the 3' end of the VH region. The entire DNA sequence of each
 30 combination was confirmed to be correct. The different deimmunized VH regions (SEQ ID NO.:70, 72, 74 and 76) and VL regions (SEQ ID NO.:78, 80 and 82) with the corresponding original non-deimmunized sequences (VH:SEQ ID NO.:110; VL:SEQ ID NO.:112) of the anti-CD3 constructs are summarized in Table 9.

Table 9. SEQ ID Nos. of deimmunized VH and VL regions

	SEQ ID NO.:		SEQ ID NO.:		SEQ ID NO.:		SEQ ID NO.:	
	Nucleic acid	Amino acid	Nucleic acid	Amino acid	Nucleic acid	Amino acid	Nucleic acid	Amino acid
Deimmunized VH2	69	70	85	86	93	94	95	96
Deimmunized VH3	71	72	85	86	93	94	95	96
Deimmunized VH5	73	74	87	88	91	92	95	96
Deimmunized VH7	75	76	87	88	89	90	95	96
VH of the non-deimmunized CD3	109	110	83	84	89	90	95	96
VH of the non-deimmunized CD3 with Cys→Ser Mutation	105	106	83	84	89	90	107	108
Deimmunized VL1	77	78	99	100	101	102	103	104
Deimmunized VL2	79	80	99	100	101	102	103	104
Deimmunized VL3	81	82	97	98	101	102	103	104
VL of the non-deimmunized CD3	111	112	97	98	101	102	103	104

1.4 Transfer of deimmunized single chain antibody genes into expression vector

- 5 The deimmunized anti-CD3 cassettes were excised from pPCR-S-Amp-SK+ with BspE1 and Sal1 and cloned into the expression vector pEF comprising VL_{CD19}-VH_{CD19}-VH_{CD3}-VL_{CD3}. The CD3 part of the pEF-DHFR vector was replaced with each of the deimmunized anti-CD3 cassettes from the BspE1 site to the Sal1 site resulting in the following 12 constructs:

10

pEF anti-CD19xanti-CD3 (VH2/VL1) (SEQ ID NOs. 177, 178)
pEF anti-CD19xanti-CD3 (VH2/VL2) (SEQ ID NOs. 179, 180)
pEF anti-CD19xanti-CD3 (VH2/VL3) (SEQ ID NOs. 181, 182)
pEF anti-CD19xanti-CD3 (VH3/VL1) (SEQ ID NOs. 183, 184)
15 pEF anti-CD19xanti-CD3 (VH3/VL2) (SEQ ID NOs. 185, 186)
pEF anti-CD19xanti-CD3 (VH3/VL3) (SEQ ID NOs. 187, 188)
pEF anti-CD19xanti-CD3 (VH5/VL1) (SEQ ID NOs. 189, 190)

- pEF anti-CD19xanti-CD3 (VH5/VL2) (SEQ ID NOs. 191, 192)
 pEF anti-CD19xanti-CD3 (VH5/VL3) (SEQ ID NOs. 193, 194)
 pEF anti-CD19xanti-CD3 (VH7/VL1) (SEQ ID NOs. 195, 196)
 pEF anti-CD19xanti-CD3 (VH7/VL1) (SEQ ID NOs. 197, 198)
 5 pEF anti-CD19xanti-CD3 (VH7/VL3) (SEQ ID NOs. 199, 200).

The constructs further comprises a murine IgG heavy chain leader in order to enable the secretion of the protein. The DNA sequences of the deimmunized anti-CD3 cassettes in the expression vector were confirmed using the sequencing primers
 10 (SEQ ID No.: 28 and 29). The DNA and amino acid sequences of the 12 deimmunized anti-CD3 cassettes in the pEF vector from the BspE1 site to the Sal1 site are shown in SEQ ID NO.:s 177-200.

1.5 Production of antibody constructs

15 After transformation of the vector into E. coli K12, transfection-grade DNAs of the different expression vectors were prepared. Secreted proteins were produced in CHO-dhfr- cells. For transient production the cell culture supernatants were harvested 2 days after transfection, for the generation of stable transfected cells, cells were put in selection medium two days after transfection. After five passages,
 20 stable pools were obtained. Subsequently, single clones were identified in limiting dilutions. To facilitate the purification process, the cells were adapted to serum-free medium. Antibody constructs were purified from about 1 liter of supernatant. The production levels were tested in ELISA. No major differences in the secreted antibody levels were observed between different constructs comprising anti-CD19
 25 and deimmunized anti-CD3 constructs.

Example 2: Binding Assays

In order to analyze the binding efficacy of the deimmunized constructs to CD3 and CD19 a FACS-based assay was performed. Initially, crude supernatants were tested
 30 for binding on CD3-enriched PBMCs or CD19-positive NALM-6 cells. Cells were incubated with non-diluted supernatants for 30 minutes at 8 °C. Upon two wash steps the cells were labeled with an anti-His antibody (Qiagen) under the same conditions. After additional wash steps binding of the constructs was detected with a FITC-conjugated sheep anti-mouse antibody (Sigma). Cells were analyzed with a FACS
 35 Calibur cytometer (B&D). As controls supernatants of anti CD19xanti CD3 and GFP-transfected cells were included. CD3 and a secondary antibody was used as a

negative control and it showed a mean fluorescence intensity (MFI) of ca. 3.5. The anti-CD19xanti-CD3 constructs comprising anti-CD3 (VH5/VL1) (SEQ ID NO.:190), anti-CD3 (VH5/VL2) (SEQ ID NO.:192), anti-CD3 (VH5/VL3) (SEQ ID NO.:194), anti-CD3 (VH7/VL1) (SEQ ID NO.:196), anti-CD3 (VH7/VL2) (SEQ ID NO.:198) and anti-CD3 (VH7/VL3) (SEQ ID NO.:200) had a MFI of at least 90, thus binding about 25 times more strongly. The positive control, which was a non-deimmunized anti-CD19xanti-CD3 construct reached a MFI of around 60 showing that the deimmunized constructs comprising anti-CD3 (VH5/VL1) (SEQ ID NO.:190), anti-CD3 (VH5/VL2) (SEQ ID NO.:192), anti-CD3 (VH5/VL3) (SEQ ID NO.:194), anti-CD3 (VH7/VL1) (SEQ ID NO.:196), anti-CD3 (VH7/VL2) (SEQ ID NO.:198) and anti-CD3 (VH7/VL3) (SEQ ID NO.:200) bound CD3 with extremely high efficacy. In a second experiment, the following constructs comprising anti-CD19 and anti CD3: anti-CD3 (VH2/VL1) (SEQ ID NO.:178), anti-CD3 (VH2/VL2) (SEQ ID NO.:180), anti-CD3 (VH2/VL3) (SEQ ID NO.:182), anti-CD3 (VH3/VL1) (SEQ ID NO.:184), anti-CD3 (VH3/VL2) (SEQ ID NO.:186) and anti-CD3 (VH3/VL3) (SEQ ID NO.:188), showed similar binding as the negative control (MFI ca. 6).

The FACS-based binding assay was also carried out for CD19. In this experiment CD19 and a secondary antibody was as a negative control. In this experiment, all assayed constructs achieved a MFI of at least 80 while the MFI of the negative control was ca. 3.

Thus, the constructs comprising anti-CD3 (VH5/VL1) (SEQ ID NO.:190), anti-CD3 (VH5/VL2) (SEQ ID NO.:192), anti-CD3 (VH5/VL3) (SEQ ID NO.:194), anti-CD3 (VH7/VL1) (SEQ ID NO.:196), anti-CD3 (VH7/VL2) (SEQ ID NO.:198) and anti-CD3 (VH7/VL3) (SEQ ID NO.:200) turned out to bind as well CD3 and CD19 as the non-modified anti CD19xanti CD3 (SEQ ID NO.:204). However, the constructs anti-CD3 (VH2/VL1) (SEQ ID NO.:178), anti-CD3 (VH2/VL2) (SEQ ID NO.:180), anti-CD3 (VH2/VL3) (SEQ ID NO.:182), anti-CD3 (VH3/VL1) (SEQ ID NO.:184), anti-CD3 (VH3/VL2) (SEQ ID NO.:186), anti-CD3 (VH3/VL3) (SEQ ID NO.:188) had completely lost anti-CD3 binding capacity, while CD19 binding was fully retained (Figure 7).

Thus, it was demonstrated that the deimmunized heavy chains dominated the binding specificity and strength. As a result, the anti-CD3 constructs with VH5 and VH7 groups were purified and analyzed for cytotoxic activity.

Example 3. Expression and purification of the variants showing high binding affinity

The deimmunized anti-CD19xanti-CD3 proteins anti-CD3 (VH5/VI1) (SEQ ID NO.:190), anti-CD3 (VH5/VI2) (SEQ ID NO.:192), anti-CD3 (VH5/VI3) (SEQ ID NO.:194), anti-CD3 (VH7/VI1) (SEQ ID NO.:196), anti-CD3 (VH7/VI2) (SEQ ID NO.:198) and anti-CD3 (VH7/VI3) (SEQ ID NO.:200) were expressed in chinese hamster ovary cells (CHO).

In order to purify the bispecific single-chain constructs comprising a deimmunized anti-CD3 part CHO-CD19 cells were grown in roller bottles with HiClone CHO modified DMEM medium (HiQ)® for 7 days before harvest. The cells were removed by centrifugation and the supernatant, containing the expressed protein was stored at -20°C.

Äkta FPLC System® (Pharmacia) and Unicorn Software® were used for chromatography. All chemicals were of research grade and purchased from Sigma (Deisenhofen) or Merck (Darmstadt).

Hydrophobic charge induction chromatography was performed on MEP Hypercel® medium loaded to a XK16/60 column (Pharmacia) that was equilibrated with buffer A1 (20 mM Tris pH 7.2). 500ml of cell culture supernatant were applied to the column (10 ml) with a flow rate of 3 ml/min. Unbound sample was washed out with buffer A1 and the bound protein was eluted with 100% buffer B1 (20 mM acetate pH 3.5). Eluted protein fractions were pooled for further purification.

IMAC was performed, using a HisTrap® column (Pharmacia) that was loaded with NiSO₄ according to the manufacturers protocol. The column was equilibrated with buffer A2 (20 mM NaP pH 7.5, 0.4 M NaCl) and the sample was diluted 2:1 with buffer A2 to obtain a pH of 7. The sample was applied to the column (2 ml) with a flow rate of 1 ml/min and the column was washed with buffer A2 to remove unbound sample. Bound protein was eluted using a 2 step gradient of buffer B2 (20 mM NaP pH 7.5, 0.4 M NaCl, 0.5 M Imidazol) Step 1: 20% buffer B2 in 10 column volumes; Step 2: 100% buffer B2 in 10 column volumes. Eluted protein fractions were pooled for further purification.

Gel filtration chromatography was performed on a Sephadex S200 HiPrep® column (Pharmacia) equilibrated with PBS (Gibco). Eluted protein samples (flow rate 1ml/min) were subjected to SDS-Page and Western Blot for detection (Figure 11).

The column was previously calibrated for molecular weight determination (molecular weight marker kit, Sigma MW GF-200).

The deimmunized variants of anti CD19 x anti CD3 protein were isolated in a three step purification process including hydrophobic charge induction chromatography (HCIC) (Figure 8), immobilized metal affinity chromatography (IMAC) (Figure 9) and gel filtration (Figure 10). The bispecific construct had a molecular weight of 52 kDa under native conditions as determined by gel filtration in PBS.

The purified bispecific protein was analyzed with SDS PAGE under reducing conditions using precast 4-12% Bis Tris gels (Invitrogen). Sample preparation and application were according to the manufacturers protocol. The molecular weight was determined with MultiMark® protein standard (Invitrogen). The gel was stained with colloidal Coomassie (Invitrogen protocol). The purity of the isolated protein was >95% (Figure 11a) and the molecule has a size of 52 kD.

Furthermore, the deimmunized variants of anti CD19 x anti CD3 protein were specifically detected by Western Blot. Western Blot was performed with an Optitran BA-S83® membrane and the Invitrogen Blot Module® according to the manufacturers protocol. The antibodies used were Penta His (Quiagen) and Goat-anti-Mouse-Ig labeled with alkaline phosphatase (AP) (Sigma), the staining solution was BCIP/NBT liquid (Sigma). The main signal was shown to correspond to the main band in the SDS PAGE at 52kD (Figure 11b).

Protein concentrations were determined using protein assay dye (MicroBCA®, Pierce) and IgG (Biorad) as standard protein. A summary of the final yields of purified protein variants is given in Table 10 showing the high productivity of all the constructs and very good yield of construct with anti CD3 (VH5/VL1) (SEQ ID NO.:190) of 924.8 µg.

Table 10. Protein yields of the deimmunized anti-CD19-anti-CD3 constructs

Deimmunized CD3 construct	Yield [µg/supernatant]
CD19xanti CD3 (VH5/ VL1)(SEQ ID NO.:190)	924.8
CD19xanti CD3 (VH5/ VL2)(SEQ ID NO.:192)	446.7
CD19xanti CD3 (VH5/ VL3)(SEQ ID NO.:194)	218.4
CD19xanti CD3(VH7/ VL1)(SEQ ID NO.:196)	268.5
CD19xanti CD3(VH7/VL2)(SEQ ID NO.:198)	553.4
CD19xanti CD3(VH7/VL3) (SEQ ID NO.:200)	477.3

The productivity of the CD19xanti CD3 (VH5/ VL2) and CD19xanti CD3(VH7/VL2) constructs was compared with the corresponding non-deimmunized constructs. The results are shown in Table 11.

5 **Table 11. Yields of the deimmunized bispecific construct compared to the corresponding non-deimmunized construct**

Construct	Yield (µg/l)
CD19xanti-CD3	62
CD19xantiCD3(VH5/VL2)	204
CD19xantiCD3(VH7/VL2)	310

10 Table 11 clearly demonstrates that the bispecific constructs comprising deimmunized CD3 binding domain have much higher (at least three fold) productivity than the corresponding non-deimmunized construct.

Example 4. FACS based binding assays of the anti-CD3 constructs

Binding of selected purified antibody constructs comprising anti-CD19 and anti-CD3 was detected as described above in Example 2 at various concentrations. In the CD3 binding assay, the negative control secondary antibody (anti-His, FITC-conjugated), which was incubated with CD3 positive cells, showed a MFI of about 2.5 and the positive control deimmunized antiCD19xanti-CD3 bispecific single chain antibody of about 70 at 1 µg/ml concentration and 50 at 5 µg/ml concentration (Figure 12A). At the concentration of 1 µg/ml, the anti-CD3 (VH5/VL1) (SEQ ID NO.:190), anti-CD3 (VH7/VL1) (SEQ ID NO.:196), anti-CD3 (VH7/VL2) (SEQ ID NO.:198) and anti-CD3 (VH7/VL3) (SEQ ID NO.:200) deimmunized bispecific antibodies showed MFI values of 10-20; anti-CD3 (VH5/VL1) (SEQ ID NO.:190) having the highest (20). At 5 µg/ml anti-CD3 (VH7/VL2) (SEQ ID NO.:198) reached a MFI of 25, while anti-CD3 (VH7/VL1) (SEQ ID NO.:196), anti-CD3 (VH7/VL3) (SEQ ID NO.:200) and anti-CD3 (VH5/VL1) (SEQ ID NO.:190) had an MFI of at least 40 thus, showing the same binding efficacy than the non-deimmunized positive control. At a concentration of 5 µg/ml the strongly binding constructs with deimmunized anti CD3 part VH5/VL1 (SEQ ID NO.:190), VH7/VL1 (SEQ ID NO.:196), VH7/VL2 (SEQ ID NO.:198), VH7/VL3 (SEQ ID NO.:200) bound to CD3 as well as the non-deimmunized anti CD19xanti CD3 (SEQ ID NO.:204).

All the antibody constructs bound to CD19 with a high efficacy, which was at about 200 MFI, while non-deimmunized anti-CD19xanti-CD3 construct (SEQ ID NO.:204)

showed 80 MFI. No differences were observed for CD19 binding at the tested concentrations for the different constructs (Figure 12B).

Example 5. Cytotoxicity Assays

- 5 anti CD19xanti CD3 mediates T cell dependent cytotoxicity to CD19-positive target cells. This was analyzed in vitro for the determination of the biological potency of anti CD19xanti CD3.

For this purposes fluorescence labeled CD19-positive NALM-6 target cells were incubated with isolated PBMC of random donors or CB15 T-cells (standardized T-cell
10 line) as effector cells in the presence of anti CD19xanti CD3. After incubation for 4 h at 37 °C in a humidified incubator, the release of the fluorescent dye from the target cells into the supernatant is determined in a spectrofluorimeter. Target cells incubated without anti CD19xanti CD3 and target cells totally lysed by the addition of saponin at the end of the incubation serve as negative and positive controls,
15 respectively. The specific cytotoxicity mediated at a certain anti CD19xanti CD3 concentration can be calculated with the following formula:

$$\text{Specific Cytotoxicity [\%]} = \frac{\text{RFU (Sample)} - \text{Mean RFU (control)}}{\text{Mean RFU (total lysis)} - \text{Mean RFU (control)}} \times 100$$

The dose response was analyzed from 0.4 pg/ml anti CD19xanti CD3 to 100 ng/ml anti CD19xanti CD3 to specify the EC50 value. Although the EC50 value describes the biological potency of anti CD19xanti CD3, the absolute value will vary
20 significantly depending on the source of the effector cells. Thus a relative potency is calculated in comparison to an anti CD19xanti CD3 reference material based on the following formula:

$$\text{Relative Potency} = \frac{\text{EC50 Sample}}{\text{EC50 Reference}}$$

The cytotoxic activities of the constructs comprising anti-CD19 and deimmunized
25 anti-CD3 are shown in Figure 13. Purified non-deimmunized anti-CD19xanti CD3 was used as control. The EC50 values of the deimmunized constructs were at a range of 21.9-81.6 pg/ml while the EC50 value of the non-deimmunized anti-CD19xanti-CD3 construct was 22.7 pg/ml. Thus, all deimmunized constructs revealed EC 50 values comparable to the non-deimmunized molecule.

Example 6. T-cell proliferation assay

Twenty healthy donors were selected for screening in T cell assays based on HLA-DR typing (Table 12). This enables the screening of peptides in the T cell assay against greater than 80% of DR alleles expressed in the world population.

5

Table 12: HLA DR haplotypes of 20 healthy donors used to test the immunogenicity of peptides obtained from deimmunized and non-deimmunized anti-CD3 scAb.

	HLA DR Allotype
1	DRB1*07, DRB1*15, DRB4*01, DRB5
2	DRB1*03, DRB1*04, DRB3, DRB4*01
3	DRB1*04, DRB1*07 and DRB4*01
4	DRB1*07, DRB1*11, DRB4*01
5	DRB1*04, DRB1*07, DRB4*01
6	DRB1*01, DRB1*04, DRB4*01
7	DRB1*03, DRB1*07, DRB3, DRB4*01
8	DRB1*07, DRB1*11, DRB3, DRB4*01
9	DRB1*12, DRB1*15, DRB3, DRB5
10	DRB1*01, DRB1*09, DRB4*01
11	DRB1*03, DRB1*15, DRB3, DRB5
12	DRB1*10, DRB1*13, DRB3
13	DRB1*03, DRB1*15, DRB3, DRB5
14	DRB1*04, DRB1*15, DRB4*01, DRB5
15	DRB1*04, DRB1*13, DRB3, DRB4*01
16	DRB1*01, DRB1*13, DRB3
17	DRB1*01, DRB1*04, DRB4*01
18	DRB1*07, DRB1*13, DRB3, DRB4*01
19	DRB1*07, DRB1*16, DRB4*01, DRB5
20	DRB1*04, DRB1*15, DRB4*01, DRB5

10

6.1 T-Cell Proliferation Assay

Peptides were obtained from Pepscan (Netherlands) at a purity of greater than 90%. Peripheral blood mononuclear cells (PBMC) from the 20 selected healthy donors (Table 12) were used to screen individual peptides in triplicate wells at 1 and 5 μ M. Two positive control peptides (C32 and C49) and keyhole limpet hemocyanin (KLH) were included in the assay. After 7 days incubation of cells and peptides, an 18 hour pulse with 3H-thymidine at 1 μ Ci/well was used to assess T cell proliferation. These data are expressed as stimulation index where:

15

Stimulation Index = CPM of test peptide / CPM of untreated control

A T cell epitope is defined as a peptide giving a stimulation index (SI) greater than 2.

The results from two independent runs indicated that 5 of the 22 MHC binding peptides in the non-deimmunized anti-CD3 sequence had the capacity to induce human T cell proliferation (SI>2). In contrast, none of the corresponding deimmunized molecules induced T cell proliferation. Table 13 summarizes the T cell proliferation assay results showing Mean SI values of 2 independent runs.

The data also showed a concentration dependent effect whereby each of the non-deimmunized binding molecules showed SI's > 2 in only one of the two concentrations (1µm or 5µm) used. The difference in response at different concentrations is explained by the fact that individual peptides will have optimum concentrations at which they induced T cell proliferation. If this concentration is exceeded, then proliferation can drop off (high peptide concentrations can have an inhibitory effect on T cell proliferation). This explains why, in some instances, proliferation is seen at the lower concentration and not at the higher. From experience, T cell proliferation will be observed at one or two of the peptide concentrations used if a peptide contains a T cell epitope. These data demonstrated that deimmunization had successfully removed T cell epitopes from anti CD3 (VH5/ML2) (SEQ ID NO.:19) and anti CD3 (VH7/ML2) (SEQ ID NO.:25). The fact that about 75% of MHC binding peptides from the non-deimmunized anti-CD3 sequence did not induce T cell proliferation can be explained either by tolerance of the human immune system to these peptides or an inability of the human T cell repertoire to recognise these particular peptides.

Table 13: Summary of data comparing positive (SI>2) mouse peptides and corresponding deimmunized peptides.

			Non-deimmunized Anti-CD3	Deimmunized Anti-CD3
Peptide Region	Allotype	Concentration (μM)	Mean SI	Mean SI
6-20	5	5	2.51	0.77
74-86	5	1	2.52	0.97
				0.96
90-102	5	5	2.21	0.56
				1.38
90-102	6	5	2.24	0.90
				0.82
90-102	11	5	2.23	0.83
				0.78
162-174	5	1	3.82	0.59
216-230	10	1	2.12	1.03

Example 7. Homology alignment of anti-CD3 (VH5), anti-CD3 (VH7), anti-CD3 (VH2) and anti-CD3 (VH3) with the non-deimmunized anti-CD3 VH

The variable heavy region of the non-deimmunized CD3 antibody, VH5 (SEQ ID NO.:74), VH7 (SEQ ID NO.:76), VH2 (SEQ ID NO.:70) and VH3 (SEQ ID NO.:72) were aligned using the AlingnX program of Vector NTI Advance (Informax, Inc., USA). The Clustal W algorithm used is described in Nucleic Acid Research, 22 (22): 4673-4860, 1994. The alignment is shown in Figure 14. From the alignment can be seen that the variable regions VH5 and VH7, which show surprisingly good binding have the sequence ASGYTF at the transition region of framework 1 to CDR1. Furthermore, the VH regions showing no binding (VH2 (SEQ ID NO:70) and VH3 (SEQ ID NO.:72)) comprise the sequence ASGYTA at the transition of framework 1 to CDR1. Thus, for obtaining a construct having reduced propensity to generate T cell epitopes and binding to CD3, the construct has to comprise the sequence ASGYTF at the transition of framework 1 to CDR1. Surprisingly, the variable heavy regions binding to CD3 and showing reduced propensity to generate T cell epitopes comprising the above-mentioned sequence ASGYTF show good binding.

Example 8. Cloning of constructs comprising deimmunized anti-CD3 and anti-EpCAM

In order to demonstrate that the deimmunized anti-CD3 polypeptide of the invention can be a part of a functional construct with other targets, a number of bispecific constructs comprising deimmunized anti-CD3 (VH5/VL2) (SEQ ID NO.:19) and different anti-EpCAM single chain antibodies (3-1 (SEQ ID NO.:137, 139), 3-5 (SEQ ID NO.:141, 143), 4-1 (SEQ ID NO.:145, 147), 4-7 (SEQ ID NO.:149, 151), 5-10 (SEQ ID NO.:133, 135)) were generated.

8.1 Cloning of C-terminal EpCAM binders comprising deimmunized anti-CD3 part (SEQ ID Nos.: 30, 31, 32, 33, 34, 35, 36, 37, 38 and 39)

8.1.1 Amplification of the deimmunized anti-CD3 from the anti-CD19xanti CD3 (VH5/VL2) construct (SEQ ID NO.:192)

The N-terminal deimmunized anti CD3(VH5/VL2) was obtained by PCR using the deimmunized (CD19 x anti-CD3 (VH5/VL2) (SEQ ID NO:192) as template and the following primers (DI CD3 5-2 VH BsrGI AGGTGTACACTCCGACGTCCAACCTGGTGCAGTCAG (SEQ ID NO.:40), DI CD3 5-2 VL BspEI AATCCGGATTGATCTCCACCTTGGTCCCG (SEQ ID NO.:41).

8.1.2. Cloning and expression of the deimmunized anti-CD3xanti-EpCAM deimmunized constructs in VH_{CD3} - VL_{CD3} x VH_{EpCAM} - VL_{EpCAM} orientation

The above mentioned PCR product containing the deimmunized anti-CD3 was cleaved with the restriction enzymes BsrG1 and BspE1 and subsequently cloned into the bluescript KS vector (Stratagene, La Jolla, CA), containing the amino acid sequence of an eukaryotic secretory signal (leader peptide) as a EcoRI/BsrGI-fragment. After cleavage of this construct with EcoRI and BspEI the resulting DNA fragment comprising the respective anti-CD3 scFv with the leader peptide was cloned into a EcoRI/BspEI cleaved plasmid containing the anti EpCAM scFv 3-1, 4-7, or 5-10 in C-terminal position in pEF-DHFR- vector. After confirmation of the sequence coding for the bispecific single chain by sequencing (Sequiseive, Vaterstetten) the plasmid was transfected into DHFR deficient CHO cells for eukaryotic expression. Eukaryotic protein expression in DHFR deficient CHO cells was performed as described in Kaufmann R.J. (1990) Methods Enzymol. 185, 537-566).

8.1.3. Cloning and expression of the deimmunized anti-CD3xanti-EpCAM constructs in VH_{CD3} - VL_{CD3} x VL_{EpCAM} - VH_{EpCAM} orientation

Anti-EpCAM 4-7 in VL-VH orientation containing the 15 amino acid standard linker (SEQ ID NO.:168) was obtained by PCR. The 4-7 VH region and the 4-7 VL region

were separately amplified by the following primers (4-7 VL: 4-7 VL BspEI FOR CTGAAATCCGGAGGTGGTGGATCCGAGCTCGTGATGACCCAGACTCC (SEQ ID NO.:117), 4-7 VL GS15 REV GGAGCCGCCGCCGCGCCAGAACCACCA CCACCTTTGATCTCAAGCTTGGTCCCC (SEQ ID NO.:118); 4-7 VH: 4-7 VH GS15

5 FOR

GGCGGCGGCGGCTCCGGTGGTGGTGGTTCTGAGGTGCAGCTGCTCGAGCAG (SEQ ID NO.:42), 4-7 VH Sall REV TTTTAAGTCGACCTAATGATGATGATGATGATGTGAGGAGACGGTGACCGTGG (SEQ ID NO.:43)). Overlapping

10 complementary sequences introduced into the PCR products were used to form the coding sequence of a 15-amino acid (G₄S₁)₃ (single-letter amino acid code) linker (standard linker) (SEQ ID NO.:168) during the subsequent fusion PCR. This amplification step was performed with the primer pair 4-7 VL BspEI FOR and 4-7 VH Sall REV (SEQ ID Ns. 42 and 43).

15 Anti-EpCAM 5-10 in VL-VH orientation containing the 15 amino acid standard ((G₄S₁)₃) linker was obtained by PCR. The 5-10 VH region and the 5-10 VL region were separately amplified by the following primers (5-10 VL: 5-10 VL BspEI FOR CTGAAATCCGGAGGTGGTGGATCCGAGCTCGTGATGACACAGTCTCCAT (SEQ ID NO.:44), 5-10 VL GS15 REV

20 GGAGCCGCCGCCGCGCCAGAACCACCACCACCTTTGATCTCAAGCTTGGTCCCAG; (SEQ ID NO.:45) 5-10 VH: 5-10 VH GS15 FOR GGCGGCGGCGGCTCCGGTGGTGGTGGTTCTGAGGTGCAGCTGCTCGAGC (SEQ ID NO.:46), 5-10 VH Sall REV

25 TTTTAAGTCGACCTAATGATGATGATGATGATGTGAGGAGACGGTGACCGTGG (SEQ ID NO.:47). Overlapping complementary sequences introduced into the PCR products were used to form the coding sequence of a 15-amino acid (G₄S₁)₃ (single-letter amino acid code) linker (standard linker) (SEQ ID NO.:168) during the subsequent fusion PCR. This amplification step was performed with the primer pair 5-10 VL BspEI FOR and 5-10 VH Sall REV.

30

The PCR products 5-10 VL-VH and 4-7 VL-VH) were cloned into the pEF-DHFR vector comprising anti-CD3 construct (VH5/VL2). After confirmation of the sequence coding for the bispecific single chain by sequencing the plasmid was transfected into DHFR deficient CHO cells for eukaryotic expression. Eukaryotic protein expression in DHFR deficient CHO cells was performed as described in Kaufmann R.J. (1990) Methods Enzymol. 185, 537-566).

35

8.1.4. Binding of the deimmunized anti-CD3xanti-EpCAM constructs to EpCAM and CD3

Binding of the bispecific single chain molecules with anti-CD3 part in N-terminal orientation to EpCAM and CD3 were confirmed by FACS analyses. For that purpose the EpCAM positive human gastric cancer cell line Kato III (ATCC HTB-103) was used. Binding of the anti-CD3 part was demonstrated on Jurkat cells (ATCC TIB 152).

Cells were cultured according to the recommendations of the supplier and a number of 200000 cells was incubated with 10µg/ml of the construct in 50µl PBS with 2%FCS (fetal calf serum). The binding of the construct was detected with an anti-His antibody (Penta-His Antibody, obtained from Quiagen, Hilden, FRG) at 2µg/ml in PBS with 2%FCS. As a second step R-Phycoerythrin-conjugated affinity purified F(ab')₂ derived from goat anti-mouse IgG, diluted 1:100 in 50µl PBS with 2% FCS (Dianova, Hamburg, FRG) was used. The samples were measured on a FACSScan (BD biosciences, Heidelberg, FRG).

Results of FACS analysis are shown in Fig. 15. All constructs comprising deimmunized anti-CD3 part showed stronger binding than the non-deimmunized anti-EpCAM (M79)xanti-CD3 bispecific single-chain antibody on EpCAM positive Katolll cells.

20

8.2 Cloning of N-terminal EpCAM binders comprising deimmunized anti-CD3 part

8.2.1 Cloning of the anti-EpCAM x anti-CD3 constructs

8.2.1.1 *Cloning of deimmunized 3-1xanti-CD3 (VH5/VL2) construct (SEQ ID NO.:48, 49):*

Deimmunized construct 3-1xanti-CD3 (VH5/VL2) (SEQ ID NO.: 48) was derived from non-deimmunized construct anti-EpCAM (3-1)xanti-CD3. The VH and VL regions of the anti-EpCAM antibody 3-1 are shown in SEQ ID NO.:137 and 139. The plasmids pEF-DHFR-3-1x anti-CD3 and pEF anti-CD3 (VH5/VL2) (SEQ ID NO.:192) were digested with BspEI and Sall (Biolabs) for the isolation of the vector and the insert anti-CD3 (VH5/VL2), respectively. The BspEI-Sall-digested vector was dephosphorylated and purified on 0.7% agarose gel, whereas the insert was purified on 1.5% agarose gel.

The purified fragment (BspEI-Sall) was subsequently cloned into the corresponding sites of the pEF-DHFR vector. The final 3-1xanti-CD3 (VH5/VL2) construct (SEQ ID NO.:48, 49) was verified by restriction digests and by DNA sequencing of the entire insert.

Cloning of the non-deimmunized 3-1xanti-CD3 construct:

For the cloning of the 3-1xanti-CD3 (VH5/VL2) construct the corresponding non-deimmunized construct was generated as follows.

The C-terminal 3-1 in VH-VL orientation was obtained by PCR for the construction of non-deimmunized 3-1 x anti-CD3 molecule. Fragments I and II comprising the 3-1 VH-VL in two parts were amplified by PCR using primer pairs me 91a (SEQ ID NO. 53) /me 90 (SEQ ID NO. 52) and me 83 (SEQ ID NO. 50) /me 84 (SEQ ID NO. 51), respectively. Hot Start PCR was done using the Expand High Fidelity System of Roche Diagnostics. 20 cycles (94°C/30 sec; 60°C/1min;72°C/1min) were used for amplification followed by one cycle of 3 min at 72°C.

PCR fragments I and II were subjected to electrophoresis on a 1.5% agarose gel. Fragments were mixed (1 ng of each) and used as a template for the next PCR reaction performed with primer pair me 91a (SEQ ID NO. 53) and me 84 (SEQ ID NO. 51) for amplification of fragment III comprising the entire 3-1. PCR was performed as described above, but with an annealing temperature of 68°C. Fragment III was purified on an agarose gel and digested with BsrGI and BspEI (Biolabs), purified and subsequently cloned into the corresponding sites of the pEF-DHFR-anti EpCAM (M79) X anti-CD3 construct. The cloned region was verified by restriction digests and by DNA-sequencing.

Sequences of the Primers used:

Me 83: 5'- GGT TCT GGC GGC GGC GGC TCC GGT GGT GGT GGT TCT GAG GTG CAG CTG CTC GA CAG TCT G -3' (SEQ ID NO. 50)

Me 84: 5'- GTG CTC CGG AGG AGA CGG TGA CCG TGG TCC CTT GGC CCC AG -3' (SEQ ID NO. 51)

Me 90: 5'- CCG GAG CCG CCG CCG CCA GAA CCA CCA CCA CCT TTG ATC TCA AGC TTG GTC CC -3' (SEQ ID NO. 52)

Me 91a: 5'- GGA TTG TAC A CTCC GA GCT CGT CAT GAC CCA GTC TCC ATC TTA TCT TGC TGC -3' (SEQ ID NO. 53)

8.2.1.2 Cloning of deimmunized 3-5xanti-CD3 (VH5/VL2) construct (SEQ ID NO.:54, 55):

The C-terminal 3-5 in VH-VL orientation was obtained by PCR for the construction of 3-5 xanti-CD3 molecule. The VH and VL regions of the anti-EpCAM antibody 3-5 are shown in SEQ ID NO.:141 and 143. The plasmids pEF-DHFR-3-5xanti-CD3 and pEF anti-CD3 (VH5/VL2) (SEQ ID NO 192) were digested with EcoRI and BspEI (Biolabs) for the isolation of the insert (3-5) and the vector respectively. The dephosphorylated vector (EcoRI and BspEI digested) and the insert were purified by agarose gel-electrophoresis.

The purified fragment (EcoRI-BspEI) was subsequently cloned into the corresponding sites of the pEF-DHFR vector. The final 3-5xanti-CD3 (VH5/VL2) (SEQ ID NO.:54) construct was verified by restriction digests.

5 *Cloning of the non-deimmunized 3-5xanti-CD3 construct:*

For cloning of the 3-5xanti-CD3 (VH5/VL2) construct the corresponding non-deimmunized construct was generated as follows.

10 Fragments I and II comprising the 3-5 in two parts were amplified by PCR according to the conditions described for 3-1xanti-CD3 using primer pairs me 81 (SEQ ID NO. 56) /me 90 (SEQ ID NO. 52) and me 83 (SEQ ID NO. 50) /me 84 (SEQ ID NO. 51) respectively. Agarose gel fragments comprising PCR fragments I and II were reamplified with primer pair me 81 (SEQ ID NO. 56) and me 84 (SEQ ID NO. 51) for amplification of fragment III comprising the entire 3-5. PCR was performed as described above. Fragment III was purified on an agarose gel and digested with

15 BssHII and BspEI (Biolabs), purified and subsequently cloned into the corresponding sites of the pEF-DHFRcloning vector. The cloned region was verified by restriction digests and by DNA-sequencing.

Sequence of the Me81 Primer (Seq ID NO.:56):

20 Me 81: 5'- GGA TGC GCG CGA GCT CGT GAT GAC CCA GAC TCCA CTC
TCC -3'

8.2.1.3 Cloning of the deimmunized 4-1xanti-CD3 (VH5/VL2) construct (SEQ ID NO.:57, 58):

25 The C-terminal 4-1 in VH-VL orientation was obtained by PCR for the construction of 4-1xanti-CD3 molecule. The VH and VL regions of the anti-EpCAM antibody 4-1 are shown in SEQ ID NO.:145 and 147. The plasmids pEF-DHFR-4-1xanti-CD3 and pEF anti-CD3 (VH5/VL2) (SEQ ID NO.:192) were digested with EcoRI and BspEI (Biolabs) for the isolation of the insert (4-1) and the vector respectively. The dephosphorylated vector (EcoRI and BspEI digested) and the insert were purified by

30 agarose gel-electrophoresis.

The purified fragment (EcoRI-BspEI) was subsequently cloned into the corresponding sites of the vector. The final construct 4-1xanti-CD3 (VH5/VL2) (SEQ ID NO.:57) was verified by restriction digests.

35 *Cloning of the non-deimmunized 4-1xanti-CD3 construct:*

For cloning of the 4-1xanti-CD3 (VH5/VL2) construct the corresponding non-deimmunized construct was generated as follows.

Fragments I and II comprising the 4-1 in two parts were amplified by PCR using primer pairs me 91a (SEQ ID NO. 53) /me 90 (SEQ ID NO. 452) and me 83 (SEQ ID NO. 50) /me 84 (SEQ ID NO. 51) with the above-mentioned conditions, respectively.

5 Agarose gel fragments comprising PCR fragments I and II were reamplified with primer pair me 92a (SEQ ID NO. 59) and me 84 (SEQ ID NO. 51) for amplification of fragment III comprising the entire 4-1. PCR was performed as described above but annealing was performed at 68°C. Fragment III was purified on an agarose gel and digested with BsrGI and BspEI (Biolabs), purified and subsequently cloned into the corresponding sites of the pEF-DHFR-anti EpCAM (M79) X anti-CD3 cloning vector
10 construct. The cloned region was verified by restriction digests and by DNA-sequencing.

Sequence of the Me92a primer (SEQ ID NO. 59):

Me 92a: 5'- GGA TTG TAC A CTCC GA GCT CGT GAT GAC ACA GTCTCC ATC CTC C -3'

15

8.1.2.4 Cloning of the deimmunized 4-7xanti-CD3 (VH5/VL2) construct (SEQ ID NO.:60, 61):

The C-terminal 4-7 in VH-VL orientation was obtained by PCR for the construction of 4-7 xanti-CD3. The VH and VL regions of the anti-EpCAM antibody 4-7 are shown in
20 SEQ ID NO.:149 and 151. The plasmids pEF-DHFR-4-7xanti-CD3 and pEF anti-CD3 VH5/VL2 (SEQ ID NO.:192) were digested with EcoRI and BspEI (Biolabs) for the isolation of the insert (4-7) and the vector respectively. The de-phosphorylated vector (EcoRI and BspEI digested) and the insert were purified by agarose gel-electrophoresis.

25 The purified fragment (EcoRI-BspEI) was subsequently cloned into the corresponding sites of the pEF-DHFR vector. The final construct 4-7xanti-CD3 (VH5/VL2) (SEQ ID NO.:60) was verified by restriction digests.

Cloning of the non-deimmunized construct 4-7xanti-CD3:

30 For cloning of the 4-7xanti-CD3 (VH5/VL2) construct the corresponding non-deimmunized construct was generated as follows.

Fragments I and II comprising the 4-7 in two parts were amplified by PCR using primer pairs me 81 (SEQ ID NO.:56) /me 90 (SEQ ID NO.:52) and me 83 (SEQ ID NO.:50) /me 84 (SEQ ID NO.:51) with the afore mentioned conditions, respectively.

35 Agarose gel fragments comprising PCR fragments I and II were reamplified with primer pair me 81 (Seq ID NO.:56) and me 84 (Seq ID NO.:51) for amplification of fragment III comprising the entire 4-7 VH and VL chain. PCR was performed as

described above. Fragment III was purified on an agarose gel and digested with BssHII and BspEI (Biolabs), purified and subsequently cloned into the corresponding sites of the pEF-DHFR cloning vector. The cloned region was verified by restriction digests and by DNA-sequencing.

5

8.1.2.5 Cloning of the deimmunized 5-10x anti-CD3 (VH5/VL2) construct (SEQ ID NO. 62, 63):

10 The C-terminal 5-10 in VH-VL orientation was obtained by PCR for the construction of 5-10 xanti-CD3 molecule. The VH and VL regions of the anti-EpCAM antibody 5-10 are shown in SEQ ID NO.:133 and 135. The plasmids pEF-DHFR-5-10xanti-CD3 and pEF anti-CD3 (VH5/VL2) (SEQ ID NO.:192) were digested with EcoRI and BspEI (Biolabs) for the isolation of the insert (5-10) and the vector respectively. The dephosphorylated vector (EcoRI and BspEI digested) and the insert were purified by agarose gel-electrophoresis.

15 The purified fragment (EcoRI-BspEI) was subsequently cloned into the corresponding sites of the pEF-DHFR vector. The final construct 5-10xanti-CD3 (VH5/VL2) (SEQ ID NO. 62) was verified by restriction digests and by DNA sequencing.

20 Cloning of the non-deimmunized 5-10xanti-CD3 construct:

For cloning the 5-10xanti-CD3 (VH5/VL2) construct the corresponding non-deimmunized construct was generated as follows.

25 Fragments I and II comprising the 5-10 in two parts were amplified by PCR using primer pairs me 92a (SEQ ID NO. 59) /me 90 (SEQ ID NO. 52) and me 83 (SEQ ID NO. 50) /me 84 (SEQ ID NO. 51) with the above mentioned conditions, respectively.

Agarose gel fragments comprising PCR fragments I and II were reamplified with primer pair me 92a SEQ ID NO. 59) and me 84 (SEQ ID NO. 51) for amplification of fragment III comprising the entire 5-10. PCR was performed as described above but annealing was performed at 68°C. Fragment III was purified on an agarose gel and digested with BsrGI and BspEI (Biolabs), purified and subsequently cloned into the corresponding sites of the pEF-DHFR-anti EpCAM (M79) x anti-CD3 cloning vector. The cloned region was verified by restriction digests and by DNA-sequencing.

35 8.2.2 Expression of anti EpCAMxdeimmunized-anti CD3 molecules with anti-EpCAM at the N-terminal position:

CHO-cells lacking DHFR gene were maintained in alpha MEM medium (Life Technologies, cat.no: 32561) supplemented with 10% fetal calf serum(Life

Technologies, heat inactivated at 65°C for 30 minutes) and with HT (Hypoxanthin and Thymidine; Life Technologies). The cells were transfected with pEF-DHFR-3-1xanti-CD3 (VH5/VL2) (SEQ ID NO. 48) and pEF-DHFR-5-10xanti-CD3 (VH5/VL2) (SEQ ID NO.:62), using Lipofectamine 2000 kit® (Invitrogen) according to the instructions provided by the Manufacturer. After 48 hrs. selection was performed in selection medium (alpha MEM medium containing heat inactivated 10% dialysed fetal calf serum (Life Technologies). After 3-4 weeks cell culture supernatant was collected and centrifuged at 4°C for 10 minutes at 300g to remove cells and cell debris. The supernatant containing the bispecific antibody was stored at -20°C till further analysis.

8.2.3 Binding assays of bispecific anti-EpCAMxanti CD3 variants:

250000 Jurkat cells (for CD3 binding) and Kato cells (for EpCAM binding) were independently incubated with cell culture supernatants (50µl) containing the bispecific construct (pEF-DHFR-3-1xanti-CD3 (VH5/VL2) (Nr.50, SEQ ID NO. 48) and pEF-DHFR-5-10xanti-CD3 (VH5/VL2) (Nr.54) (SEQ ID NO.:62), respectively) for 45 min. at 4°C. Thereafter, the cells were washed twice in FACS buffer (phosphate-buffered saline containing 1% fetal calf serum (FCS) and 0.05% sodium azide) and incubated with mouse anti-His antibody (Dianova, DIA910) for 60 min. at 4°C. Washing steps were performed as above.

The cells were finally incubated either with goat anti-mouse Ig-FITC-conjugated antibody (BD 550003) or with anti-mouse IgG conjugated with PE (Sigma, P8547). After washing steps, 10000 events were analysed using FACS Calibur (B&D). The results of the binding assays are shown in Figure 16. The constructs 3-1xanti-CD3 (VH5/VL2) (SEQ ID NO.:49) and 5-10xanti-CD3 (SEQ ID NO.:63) showed strong binding to CD3 on Jurkat cells and to CD19 on Kato cells.

Example 8.3. Purification of bispecific anti EpCAM constructs with deimmunized anti-CD3 part

The constructs comprising a deimmunized anti-CD3 region and an EpCAM-specific region were purified with a two-step purification process including immobilized metal affinity chromatography (IMAC) and gel filtration. Metal affinity chromatography (IMAC) and gel filtration were carried out as demonstrated in example 3.2.

A further high-resolution cation exchange chromatography was performed on a MiniS column (Amersham), equilibrated with 20mM MES buffer pH 5.5. The sample was diluted 1:3 with the same buffer before loading to the column. Bound protein was eluted with a 0-30% gradient gradient of 1 M NaCl in equilibration buffer. The eluted protein fractions were tested in the bioactivity assay. Table 14 shows the yields of the purified deimmunized EpCAM constructs. All the constructs could be efficiently

produced. Surprisingly, the construct 5-10xanti-CD3 (VH5/VL2) (SEQ ID NO.:63) had an extremely good yield of 2200 µg/l.

Table 14. Yields of the deimmunized EpCAM constructs

Construct	Yield of the monomer [µg purified protein per liter culture]
anti-CD3 (VH5/VL2)x4-7 (SEQ ID NO.:33)	112.5
3-1xanti-CD3 (VH5/VL2) (SEQ ID NO.:49)	87.5
anti-CD3 (VH5/VL2)x3-1 (SEQ ID NO.:31)	442.5
5-10xanti-CD3 (VH5/VL2) (SEQ ID NO.:63)	2200
anti-CD 3 (VH5/VL2)x5-10 (SEQ ID NO.:37)	80

Example 8.4 Cytotoxic assays of the bispecific anti-EpCAM constructs with deimmunized anti-CD3 part

In order to confirm the high bioactivity of the bispecific antibodies of the invention, a FACS based assay was carried out. CHO cells were transfected with epithelial cell adhesion molecule (EpCAM). A cell clone derived from this transfection, referred to as CHO-EpCAM cells, was used for the experiments.

For the cytotoxicity test, CHO-EpCAM (1.5×10^7) cells were washed free of serum two times with PBS and incubated with PKH26 dye (Sigma-Aldrich Co.) according to the manufacturers instructions. After staining, cells were washed two times with RPMI/10% FCS.

Cells were counted and mixed with CB15 effector cells. The CD4-positive T cell clone CB15 was kindly provided by Dr. Fickenscher, University of Erlangen/Nuernberg, Germany. Cells were cultured as recommended by the suppliers. The resulting cell suspension contained 400.000 target and 2×10^6 effector cells per ml. 50 µl of the mixture was used per well in a 96 well round bottom plate.

Antibodies were diluted in RPMI/10% FCS to the required concentration and 50 µl of this solution was added to the cell suspension. A standard reaction was incubated for 16 h at 37°C / 5% CO₂. Propidium iodide was added to a final concentration of 1 µg/ml. After 10 min of incubation at room temperature cells were analysed by FACS. PKH26 fluorescence was used for positive identification of target cells. Cytotoxicity was measured as ratio of PI positive over all target cells.

Sigmoidal dose response curves typically had R² values >0.97 as determined by Prism Software (GraphPad Software Inc., San Diego, USA). The results of the cytotoxic assays are shown in Figures 17 and 18.

Example 8.5. Comparison of the productivity of bispecific molecules comprising an EpCAM binding part and a deimmunized CD3 binding part in CHO cells

- 5 In order to determine the productivity of a deimmunized construct protein L ELISA was performed. The productivity data was calculated from batch cultures.

8.5.1 Cell Culture

10 CHO cell lines producing deimmunized (CHO-DHFR-) and non-deimmunized (CHO-DHFR- or CHO-K1) were cultivated in HyQ PF CHO LS medium + 4 mM L-Glutamine in a CO₂ incubator at 37°C and 5% CO₂. Cell numbers and viability were determined using Trypan Blue. Cell density was set to $1-2 \times 10^5$ cell/ml.

15 Cells were transferred to spinner flasks and thus adjusted to conditions of a stirred culture. Operational parameter settings were 80 rpm, 37°C and 5% CO₂ with gassing in a CO₂ incubator. Culture volume was in the 100–500 ml-range and cell density at inoculation in the range of $1-2 \times 10^5$ cells/ml. As for the subcultivation in T-flasks, cultures were centrifuged and resuspended in fresh pre-warmed medium at each passage. Cell density was set to $1-2 \times 10^5$ cells/ml.

20 For analysis of productivity data (Table 15) cells were cultivated up to 14 days (d) without any medium addition or exchange. Cell numbers and viability were determined daily using Trypan blue stain. Product concentrations in the supernatant were analyzed by Protein L ELISA.

8.5.2 Protein L ELISA

25 Quantitative binding of the bispecific molecules was carried out with rProtein L-coated microtiter plates. rProtein L is a recombinant form of the immunoglobulin-binding Protein L produced by *Peptostreptococcus magnus*. It has four binding domains and binds immunoglobulin through the light chain (κ). Bispecific molecules, which contain variable domains from two different light chains respectively parent
30 antibodies, are also bound by rProtein L.

Microtiter plates were coated with rProtein L in PBS buffer (2 μ g rProtein L/ml PBS buffer) overnight at 2–8°C. Following coating, remaining adsorption sites were blocked with of blocking buffer (2% BSA in PBS buffer). Then, the plates were frozen and stored at $\leq 18^\circ\text{C}$. Before use, the plates were thawed and washed with washing
35 buffer (0.05% Tween 20 in PBS buffer) to remove the mixture of coating solution and blocking buffer.

Serial dilutions of cell-free cell culture supernatant in 1% BSA + 0.01% Tween 20 in PBS (dilution buffer) were analyzed. Bispecific anti-EpCAM(M79)xanti-CD3 was used as positive control in comparable dilutions.

Incubation was performed overnight at 2-8°C.

- 5 After washing rabbit anti-mouse IgG (1:5,000 in dilution buffer) was added and incubated for 60 min at room temperature. Goat anti-rabbit IgG labeled with alkaline phosphatase was added (1:1,000 in dilution buffer; 60 min at room temperature) after washing. pNPP substrate solution was added and the reaction was stopped by addition of 3 M NaOH. Absorbance was measured with an ELISA reader at 405 nm
10 (reference filter 492 nm).

Table 15. Productivity of an deimmunized anti-EpCAM construct

Construct	M79xanti-anti-CD3		5-10xanti-CD3 (VH5/VL2)
	CHO-K1	CHO-dhfr-	CHO-dhfr-
Basic cell line	CHO-K1	CHO-dhfr-	CHO-dhfr-
Specific productivity	0.2-0.6 pg/cell per day	1-3 pg/cell per day	15-20 pg/cell per day
Maximal density	cell 3x10 ⁶ c/ml	1.2-1.8x10 ⁶ c/ml	1.5x10 ⁶ c/ml
Doubling time	17-20 h	25-30 h	25-30 h

- 15 Thus, the inventive 5-10xanti-CD3 (VH5/VL2) construct demonstrated much higher specific productivity (at least five times higher) than the prior art bispecific non-deimmunized EpCAM and CD3 binding antibody.

16. Okt. 2003

Claims

1. A cytotoxically active CD3 specific binding construct comprising a first domain specifically binding to human CD3 and an Ig-derived second binding domain,
5 wherein said first domain is deimmunized and comprises a CDR-H1 region, a CDR-H2 region and a CDR-H3 region, said CDR-H3 region comprising an amino acid sequence as depicted in SEQ ID NO. 96, 108, 119, 120, 121, 122, 123, 124, 125, 126, or 127; and
10 wherein said first domain further comprises in its framework H1 the sequence VKK and wherein the transition sequence between framework H1 and CDRH1 region comprises the sequence Ala-Ser-Gly-Tyr-Thr-Phe (ASGYTF; SEQ ID NO: 233).
2. The cytotoxically active CD3 specific binding construct of claim 1 further
15 comprising in said first domain a framework H3 comprising the sequence Met-Glu-Leu-Ser (MELS; SEQ ID NO: 234).
3. The cytotoxically active CD3 specific binding construct of claim 1 or 2 further
20 comprising in said first domain a framework H3 comprising the sequence Ile-Thr-Thr-Asp-Lys (ITTDK; SEQ ID NO: 235).
4. The CD3 specific binding construct of any one of claims 1 to 3, wherein said
25 first domain which specifically binds to human CD3 comprises a framework H1 as shown in SEQ ID NO. 152 or 153.
5. The CD3 specific binding construct of any one of claims 1 to 4, wherein said
first domain which specifically binds to human CD3 comprises a framework H2 as shown in SEQ ID NO. 156 or 157.
- 30 6. The CD3 specific binding construct of any one of claims 1 to 5, wherein said first domain which specifically binds to human CD3 comprises a framework H3 as shown in SEQ ID NO. 160 or 161.

7. The CD3 specific binding construct of any one of claims 1 to 6, wherein said first domain which specifically binds to human CD3 comprises a framework H4 as shown in SEQ ID NO. 164 or 165.

5 8. The CD3 specific binding construct of any one of claims 1 to 7, wherein said construct comprises

- (a) a CDR-H1 as depicted in SEQ ID NO 88; and
- (b) a CDR-H2 as depicted in SEQ ID NO 90 or 92.

10 9. The CD3 specific binding construct of any one of claims 1 to 8, wherein said construct comprises a V_H-region as depicted in SEQ ID NO.74 or 76.

10. The CD3 specific binding construct of any one of claims 1 to 9, wherein said construct comprises a CDR-L1 as depicted in SEQ ID NO. 98 or 100.

15 11. The CD3 specific binding construct of any one of claims 1 to 10, wherein said construct comprises a CDR-L2 as depicted in SEQ ID NO.102.

20 12. The CD3 specific binding construct of any one of claims 1 to 11, wherein said construct comprises a CDR-L3 as depicted in SEQ ID NO.104.

25 13. The CD3 specific binding construct of any one of claims 1 to 12 comprising a V_L region in its CD3-specific portion, wherein said V_L region is selected from the group consisting of SEQ ID NO 78, SEQ ID NO 80, SEQ ID NO 82 and SEQ ID NO 112.

----- 14. -----The CD3 specific binding construct of any of claims 1 to 13, wherein said Ig-derived second domain is a scFv.

30 15. The CD3 specific binding construct of any of claims 1 to 14, wherein said Ig-derived second domain and/or (a) connecting linker-region(s) is/are humanized and/or deimmunized.

16. The CD3 specific binding construct of any of claims 1 to 15, wherein said Ig-

derived second domain comprises an antigen-interaction-site with specificity for a cell surface molecule.

5 17. The CD3 specific binding construct of claim 16, wherein said cell surface molecule is a tumor specific marker.

10 18. The CD3 specific binding construct of any of claims 16 or 17, wherein said Ig-derived second binding domain comprises an antigen-interaction site with a specificity for a molecule selected from the group consisting of EpCAM, CCR5, CD19, HER-2, HER-2 neu, HER-3, HER-4, EGFR, PSMA, CEA,, MUC-1 (mucin), MUC2, MUC3, MUC4, MUC5_{AC}, MUC5_B, MUC7, β hCG, Lewis-Y, CD20, CD33, CD30, ganglioside GD3, 9-O-Acetyl-GD3, GM2, Globo H, fucosyl GM1, Poly SA, GD2, Carboanhydrase IX (MN/CA IX), CD44v6, Sonic Hedgehog (Shh), Wue-1, Plasma Cell Antigen, (membrane-bound) IgE, 15 Melanoma Chondroitin Sulfate Proteoglycan (MCSP), CCR8, TNF-alpha precursor, STEAP, mesothelin, A33 Antigen, Prostate Stem Cell Antigen (PSCA), Ly-6; desmoglein 4, E-cadherin neo-epitope, Fetal Acetylcholine Receptor, CD25, CA19-9 marker, CA-125 marker and Muellierian Inhibitory Substance (MIS) Receptor type II, sTn (sialylated Tn antigen, TAG72), FAP 20 (fibroblast activation antigen), endosialin, EGFRvIII, L6, SAS, CD63, TAG72, TF-antigen, Cora antigen, CD7, CD22, Ig α , Ig β , G250, gp100, MT-MMPs, F19-antigen, CO-29 and EphA2.

25 19. The CD3 specific binding construct of any of claims 1 to 18, wherein said second Ig-derived binding domain comprises an antigen-interaction site with a specificity for EpCAM.

30 20. The CD3 specific binding construct of claim 19, wherein said CD3-specific binding construct comprises an amino acid sequence selected from the group of

- (a) an amino acid sequence as shown in any one of SEQ ID NO 31, 33, 35, 37, 39, 49, 55, 58, 61, 63, 65, 67, 237, 239, 241, 243, 245, 247, 249, 251, 253, 255, 257, 259, 261, 263, 265, 267, 269, 271, 273, 275, 277,

279, 281, 283, 285, 287, 289, 291, 293, 295, 297, 299, 301, 303, 305, 307, 309, 311, 313, 315, 317, 319, 321, 323 and 325;

(b) an amino acid sequence encoded by a nucleic acid sequence as shown in any one of SEQ ID NO 30, 32, 34, 36, 38, 48, 54, 57, 60, 62, 64, 66, 236, 238, 240, 242, 244, 246, 248, 250, 252, 254, 256, 258, 260, 262, 264, 266, 268, 270, 272, 274, 276, 278, 280, 282, 284, 286, 288, 290, 292, 294, 296, 298, 300, 302, 304, 306, 308, 310, 312, 314, 316, 318, 320, 322 and 324; and

(c) an amino acid sequence encoded by a nucleic acid sequence which is degenerate as a result of the genetic code to a nucleotide sequence of (b);

(d) and amino acid sequence encoded by a nucleic acid sequence hybridising with the complementary strand of a nucleic acid sequence as defined in (b) under stringent hybridisation conditions.

21. The CD3 specific binding construct of any of claims 1 to 18, wherein said Ig-derived second binding domain comprises an antigen-interaction site with a specificity CCR5.

22. The CD3 specific binding construct of claim 21, wherein said CD3-specific binding construct comprises an amino acid sequence selected from the group of

(a) an amino acid sequence as shown in any one of SEQ ID NO 206, 208, 210, 212, 214 or 216;

(b) an amino acid sequence encoded by a nucleic acid sequence as shown in any one of in SEQ ID NO 205, 207, 209, 211, 213 or 215; and

(c) an amino acid sequence encoded by a nucleic acid sequence which is degenerate as a result of the genetic code to a nucleotide sequence of (b);

(d) and amino acid sequence encoded by a nucleic acid sequence hybridising with the complementary strand of a nucleic acid sequence as defined in (b) under stringent hybridisation conditions.

23. The CD3 specific binding construct of any of claims 1 to 18, wherein said Ig-derived second binding domain comprises an antigen-interaction site with a specificity for CD19.

5 24. The CD3 specific binding construct of claim 23, wherein said CD3-specific binding construct comprises an amino acid sequence selected from the group of

10 (a) an amino acid sequence as shown in any one of SEQ ID NO 190, 192, 194, 196, 198, 200, 327, 329, 331, 333, 335, 337, 339, 341, 343, 345, 347, 349, 351, 353, 357, 359, 361, 363, 365, 367, 369, 371, 373, 375, 377, 379, 381, 383, 385, 387, 389, 391, 393, 395, 397, 399, 401, 403, 405, 407 or 409;

15 (b) an amino acid sequence encoded by a nucleic acid sequence as shown in any one of in SEQ ID NO 189, 191, 193, 195, 197, 199, 326, 328, 330, 332, 334, 336, 338, 340, 342, 344, 346, 348, 350, 352, 354, 356, 358, 360, 362, 364, 366, 368, 370, 372, 374, 376, 378, 380, 382, 384, 386, 388, 390, 392, 394, 396, 398, 400, 402, 404, 406 or 408; and

20 (c) an amino acid sequence encoded by a nucleic acid sequence which is degenerate as a result of the genetic code to a nucleotide sequence of (b);

(d) and amino acid sequence encoded by a nucleic acid sequence hybridising with the complementary strand of a nucleic acid sequence as defined in (b) under stringent hybridisation conditions.

25 25. The CD3 specific binding construct of any of claims 1 to 18, wherein said Ig-derived second binding domain comprises an antigen-interaction site with a specificity for CD20.

30 26. The CD3 specific binding construct of claim 25, wherein said CD3-specific binding construct comprises an amino acid sequence selected from the group of

(a) an amino acid sequence as shown in any one of SEQ ID NO 218, 220, 222, 224, 226, or 228;

- (b) an amino acid sequence encoded by a nucleic acid sequence as shown in any one of in SEQ ID NO 217, 219, 221, 223, 225 or 227; and
- (c) an amino acid sequence encoded by a nucleic acid sequence which is degenerate as a result of the genetic code to a nucleotide sequence of (b);
- (d) and amino acid sequence encoded by a nucleic acid sequence hybridising with the complementary strand of a nucleic acid sequence as defined in (b) under stringent hybridisation conditions.

- 10 27. A nucleic acid sequence encoding a CD3 specific binding construct according to any of claims 1 to 26.
28. A vector comprising a nucleic acid sequence according to claim 27.
- 15 29. The vector of claim 28, which further comprises a nucleic acid sequence which is a regulatory sequence operable linked to said nucleic acid sequence according to claim 27.
30. The vector of claim 28 or 29, wherein the vector is an expression vector.
- 20 31. A host transformed or transfected with a vector according to any of claims 28 to 30.
- 25 32. A process for the production of a CD3 specific binding construct according to any of claims 1 to 26 said process comprising culturing a host of claim 31 under conditions allowing the expression of the polypeptide construct and recovering the produced polypeptide construct from the culture.
- 30 33. A composition comprising a CD3 specific binding construct according to any of claims 1 to 26 or as produced by the process of claim 32, a nucleic acid molecule of claim 27, a vector of any one of claims 28 to 30 or a host of claim 31 and, optionally, a proteinaceous compound capable of providing an activation signal for immune effector cells.

34. The composition of claim 33, which is a pharmaceutical composition further comprising, optionally, suitable formulations of carrier, stabilizers and/or excipients.
- 5 35. The composition of claim 33, which is a diagnostic composition further comprising, optionally, means and methods for detection.
- 10 36. Use of a CD3 specific binding construct according to any of claims 1 to 26 or as produced by the process of claim 32, a nucleic acid molecule of claim 27, a vector of any one of claims 28 to 30 or a host of claim 31 for the preparation of a pharmaceutical composition for the prevention, treatment or amelioration of a proliferative disease, a tumorous disease, an inflammatory disease, an immunological disorder, an autoimmune disease, an infectious disease, viral disease, allergic reactions, parasitic reactions, graft-versus-host diseases or host-versus-graft diseases.
- 15
- 20 37. A method for the prevention, treatment or amelioration of a proliferative disease, a tumorous disease, an inflammatory disease, an immunological disorder, an autoimmune disease, an infectious disease, viral disease, allergic reactions, parasitic reactions, graft-versus-host diseases or host-versus-graft diseases comprising the administration of a CD3 specific binding construct according to any of claims 1 to 26 or as produced by the process of claim 32, a nucleic acid molecule of claim 27, a vector of any one of claims 28 to 30 or a host of claim 31 to a subject in need of such a prevention, treatment or amelioration.
- 25
38. The method of claim 37, wherein said subject is a human.
- 30 39. The method of any one of claims 37 or 38 further comprising, the administration of a proteinaceous compound capable of providing an activation signal for immune effector cells.

40. The method of claim 39, wherein said proteinaceous compound is administered simultaneously or non-simultaneously with a CD3 specific binding construct according to any of claims 1 to 26 or as produced by the process of claim 32, a nucleic acid molecule of claim 27, a vector of any one of claims 28 to 30 or a host of claim 31.

41. A kit comprising a CD3 specific binding construct according to any of claims 1 to 26 or as produced by the process of claim 32, a nucleic acid molecule of claim 27, a vector of any one of claims 28 to 30 or a host of claim 31.

16. Okt. 2003

Abstract

The present invention provides a cytotoxically active CD3 specific binding construct
5 comprising a first domain specifically binding to human CD3 and an Ig-derived
second binding domain. Furthermore, a nucleic acid sequence encoding a CD3
specific binding construct of the invention is provided. Further aspects of the
invention are vectors and host cells comprising said nucleic acid sequence, a
process for the production of the construct of the invention and composition
10 comprising said construct. The invention also provides the use of said constructs for
the preparation of pharmaceutical compositions for the treatment of particular
diseases, a method for the treatment of particular diseases and a kit comprising the
binding construct of the invention.

Figure 1

Anti-CD3 WT

GATATCAAACTGCAGCAGTCAGGGCTGAACTGGCAAGACCTGGGGCCTCAGTGAAGATGTCCT
GCAAGACTTCTGGCTACACCTTTACTAGGTACGATGCACCTGGGTAAACAGAGCCTGGACA
GGTCTGGAATGGATTGGATACATTAAATCCTAGCCGTGTTATACTAATAATACAATCAGAAATT
AAGGACAAGGCCACATTGACTACAGACAAATCCTCAGCACAGCCTACATGCAACTGAGCAGCC
TGACATCTGAGGACTCTGCAGTCTATTACTGTGCAAGATATTATGATGATCATTACTGCCTTGA
CTACTGGGCCAAGGCACCACTCTCACAGTCTCCTCAGTCGAAAGTGGAGTTCCTGCTGGT
GGAAGTGGAGGTTCAAGTGGAGTCGACGACATTCAAGTCACTCAGCTCCAGCAATCATGTCTG
CATCTCCAGGGAGAAGGTACCATGACCTGCAGAGCCAGTTCAAGTGTAAAGTTACATGAAC
GTACCAGCAGAAGTCAGGCACCTCCCCAAAGATGGATTATGACACATCCAAGTGGCTTCT
GGAGTCCCTTATCGCTTCAGTGGCAGTGGGTCTGGACCTCATACTCTCACAAATCAGCAGCA
TGGAGGCTGAAGATGCTGCCACTTATTACTGCCAACAGTGGAGTAGTAACCCGCTCACGTTCCG
TGCTGGGACCAAGCTGGAGCTGAAA

AA Sequence

DIKLQQSGAELARPGASVKMSCKTSGYTFTRYTMHWVKQRPQGQLEWIGYINPSRGYTNYNQKF
KDKATLTIDKSSSTAYMQLSSLTSEDSAVYYCARYYDDHYCLDYWGQGTTLTVSSVEGGSGSG
GSGSGGVDDIQLTQSPAIMASPGEKVTMTCRASSVSVMNWYQQKSGTSPKRWIYDTSKVAS
GVPYRFGSGSGTSYSLTISSEAEADAATYYCQQWSSNPLTFGAGTKLELK

Fig. 2 A

VH2

DVQLVQSGAEVKKPGASVKVSCKASGYTATRYTMHWVRQAPGQGLEWIGYINPSR
GYTNYAQKLQGRVTMTTDTSTAYMELSSLRSEDATYYCARYYDDHYCLDYWG
QGTTVTVSS

VH3

DVQLVQSGAEVKKPGASVKVSCKASGYTATRYTMHWVRQAPGQGLEWIGYINPSR
GYTNYAQKLQGRVTMTTDTSTAYLQMNSLKTEDTAVYYCARYYDDHYCLDYWG
QGTTVTVSS

VH5

DVQLVQSGAEVKKPGASVKVSCKASGYTFTRYTMHWVRQAPGQGLEWIGYINPSR
GYTNYADSVKGRFTITTDKSTSTAYMELSSLRSEDATYYCARYYDDHYCLDYWG
QGTTVTVSS

VH7

DVQLVQSGAEVKKPGASVKVSCKASGYTFTRYTMHWVRQAPGQGLEWIGYINPSR
GYTNYNQKFKDRVTITTDKSTSTAYMELSSLRSEDATAVYYCARYYDDHYCLDYWG
QGTTVTVSS

Fig. 2 A (cont.)

VL1

DIQMTQSPSSLASVGDRVTITCRASQSVSYMNWYQQKPGKAPKRWIYDT
SKVASGVPARFSGSGTDYSLTINSLEAEDAATYYCQQWSSNPLTFGGG
TKVEIK

VL2

DIVLTQSPATLSLSPGERATLSCRASQSVSYMNWYQQKPGKAPKRWIYDT
SKVASGVPARFSGSGTDYSLTINSLEAEDAATYYCQQWSSNPLTFGGG
TKVEIK

VL3

DIVLTQSPATLSLSPGERATLTCRASSVSYMNWYQQKPGKAPKRWIYDT
SKVASGVPARFSGSGTDYSLTINSLEAEDAATYYCQQWSSNPLTFGGG
TKVEIK

Fig. 2 B

VH2

GACGTCCAAC TGGTGAGT CAGGGGCT GAAGTG AAAAAC CTGGGGCT CAGTGA AGGTGTCCTGC
AAGGCTTCTG GCTACACCGCTA CTAGTACG ATGCAC TGGTAAGGCAGGCACCTGGACAGGGT
CTGGAATGGAT TGGATACATTA ATCCTAGCCG TGTATACTA ATTAACGCACAGAA GTTGCAGGGC
CGCGTCACAA TGACTACAGACACTTCC ACCAGCACAG CCTACATGGA ACTGAGCAGCCTGCGTTCT
GAGGACACTGCA ACCTATTACT GTGCAAGATA TTATGATGATCAT TACTGCCCTTGACTACTGGGGC
CAAGGCACCACG GTCACCGTCTCCTCA

VH3

GACGTCCAAC TGGTGAGT CAGGGGCT GAAGTG AAAAAC CTGGGGCT CAGTGA AGGTGTCCTGC
AAGGCTTCTG GCTACACCGCTA CTAGTACG ATGCAC TGGTAAGGCAGGCACCTGGACAGGGT
CTGGAATGGAT TGGATACATTA ATCCTAGCCG TGTATACTA ATTAACGCACAGAA GTTGCAGGGC
CGCGTCACAA TGACTACAGACACTTCC ACCAGCACAG CCTACCTGCA AATGAACAGCCTGAAA ACT
GAGGACACTGCA GTCTATTACT GTGCAAGATA TTATGATGATCAT TACTGCCCTTGACTACTGGGGC
CAAGGCACCACG GTCACCGTCTCCTCA

VH5

GACGTCCAAC TGGTGAGT CAGGGGCT GAAGTG AAAAAC CTGGGGCT CAGTGA AGGTGTCCTGC
AAGGCTTCTG GCTACACCGCTT TACTAGGTACACG ATGCAC TGGTAAGGCAGGCACCTGGACAGGGT
CTGGAATGGAT TGGATACATTA ATCCTAGCCG TGTATACTA ATTAACGCACAGCGTCAAGGGC
CGCTTCACAA TCAC TACAGACAAATCC ACCAGCACAG CCTACATGGA ACTGAGCAGCCTGCGTTCT
GAGGACACTGCA ACCTATTACT GTGCAAGATA TTATGATGATCAT TACTGCCCTTGACTACTGGGGC
CAAGGCACCACG GTCACCGTCTCCTCA

Fig. 2 B (cont.)

VH7

GACGTCCAAC TGGTGCAGTCAGGGGCTGAAGTGAAAAACCTGGGGCCTCAGTGAAGGTCTCTGC
AAGGCTTCTGGCTACACCTTTACTAGGTACACGATGCACTGGGTAAAGCAGGCACCTGGACAGGGT
CTGGAATGGATTGGATACATTAAATCCTAGCCGTTACTAATTACAATCAGAAGTTC AAGGAC
CGCGTCACAATCACTACAGACAAATCCACGACAGCCTACATGGAAC TGAAGCAGCCTGCGTTCT
GAGGACACTGCAGTCTATTACTGTGCAAGATATTATGATGATCAT TACTGCCTTGACTACTGGGGC
CAAGGCACCACGGTCACCGTCTCCTCA

Fig. 2 B (cont.)

VL1

GACATTCAGATGACCCAGTCTCCATCTAGCCCTGTCTGCATCTGTCCGGGACCGTGTCACCATCACC
TGCAGAGCCAGTCAAAGTGTAAGTTACATGAACCTGGTACCAGACAGAGCCGGGCAAGGCACCCCAA
AGATGGATTATGACACATCCAAGTGGCTTCTGGAGTCCCTGCTCGCTTCAGTGGCAGTGGGTCT
GGGACCGACTACTCTCACAAATCAACAGCTTGGAGGCTGAAGATGCTGCCACTTATTACTGCCAA
CAGTGGAGTAGTAACCGCTCACGTTCCGTGGCGGGACCAAGGTGGAGATCAAA

VL2

GACATTGTAAGTACCCAGTCTCCAGCAACTCTGTCTCTGTCTCCAGGGGAGCGTGCCACCCCTGAGC
TGCAGAGCCAGTCAAAGTGTAAGTTACATGAACCTGGTACCAGACAGAGCCGGGCAAGGCACCCCAA
AGATGGATTATGACACATCCAAGTGGCTTCTGGAGTCCCTGCTCGCTTCAGTGGCAGTGGGTCT
GGGACCGACTACTCTCACAAATCAACAGCTTGGAGGCTGAAGATGCTGCCACTTATTACTGCCAA
CAGTGGAGTAGTAACCCGCTCACGTTCCGTGGCGGGACCAAGGTGGAGATCAAA

VL3

GACATTGTAAGTACCCAGTCTCCAGCAACTCTGTCTCTGTCTCCAGGGGAGCGTGCCACCCCTGACC
TGCAGAGCCAGTCAAAGTGTAAGTTACATGAACCTGGTACCAGACAGAGCCGGGCAAGGCACCCCAA
AGATGGATTATGACACATCCAAGTGGCTTCTGGAGTCCCTGCTCGCTTCAGTGGCAGTGGGTCT
GGGACCGACTACTCTCACAAATCAACAGCTTGGAGGCTGAAGATGCTGCCACTTATTACTGCCAA
CAGTGGAGTAGTAACCCGCTCACGTTCCGTGGCGGGACCAAGGTGGAGATCAAA

Fig. 2 C

vH CDR1

Wt anti-CD3
VH2, 3
VH5, 7

GYTFTRYTMH
GYTATRYTMH
GYTFTRYTMH

vH CDR2

WT anti-CD3,
VH7
VH5
VH2, 3

YINPSRGYTNYNQKFKD
YINPSRGYTNYADSVKG
YINPSRGYTNYAQKLQG

vH CDR3

WT anti-CD3,
VH2, 3, 5, 7

YYDDHYCLDY

vK CDR1

WT anti-CD3,
VL3
VL1, 2

RASSSVSYMN
RASQSVSYMN

vK CDR2

WT anti-CD3,
VL1, 2, 3

DTSKVAS

vK CDR3

WT anti-CD3,
VL1, 2, 3

QQWSSNPLT

Fig. 2 D

vH CDR1

WT anti-CD3

GGCTACACCTTTACTAGGTACACGATG
CAC

VH2, 3

GGCTACACCGCTACTAGGTACACGATG
CAC

VH5, 7

GGCTACACCTTTACTAGGTACACGATG
CAC**vH CDR2**WT anti-CD3,
VH7TACATTAATCCTAGCCGTGGTTATACT
AATTACAATCAGAAGTTCAAGGAC

VH5

TACATTAATCCTAGCCGTGGTTATACT
AATTACGCAGACAGCGTCAAGGGC

VH2, 3

TACATTAATCCTAGCCGTGGTTATACT
AATTACGCACAGAAGTTGCAGGGC**VH CDR3**WT anti-CD3,
VH2, 3,
VH5, 7TATTATGATGATCATTACTGCCTT
GACTAC

Fig. 2 D (cont.)

vK CDR1WT anti-CD3,
VL3AGAGCCAGTTCAAGTGTAAGTTACATG
AAC

VL1, 2

AGAGCCAGTCAAAGTGTAAGTTACATG
AACvK CDR2WT anti-CD3,
VL1-3

ACACATCCAAAGTGGCTTCT

VK CDR3WT anti-CD3,
VL1-3

CAACAGTGGAGTAGTAACCCGCTCACG

Figure 3**A) anti-CD3 (VH2/VL1)**

GACGTCCAACCTGGTGCAGTCAGGGGCTGAAGTGAAAAAACC
TGGGGCCTCAGTGAAGGTGTCCTGCAAGGCTTCTGGCTACA
CCGCTACTAGGTACACGATGCACTGGGTAAGGCAGGCACCT
GGACAGGGTCTGGAATGGATTGGATACATTAATCCTAGCCG
TGGTTATACTAATTACGCACAGAAGTTGCAGGGGCCGCGTCA
CAATGACTACAGACACTTCCACCAGCACAGCCTACATGGAA
CTGAGCAGCCTGCGTTCTGAGGACACTGCAACCTATTACTG
TGCAAGATATTATGATGATCATTACTGCCTTGACTACTGGG
GCCAAGGCACCACGGTCACCGTCTCCTCAGGCGAAGGTACT
AGTACTGGTTCTGGTGGAAAGTGGAGGTTGAGGTGGAGCAGA
CGACATTCAGATGACCCAGTCTCCATCTAGCCTGTCTGCAT
CTGTCGGGGACCGTGTCACCATCACCTGCAGAGCCAGTCAA
AGTGTAAGTTACATGAACTGGTACCAGCAGAAGCCGGGGCAA
GGCACCCAAAAGATGGATTTATGACACATCCAAAGTGGCTT
CTGGAGTCCCTGCTCGCTTCAGTGGCAGTGGGTCTGGGACC
GACTACTCTCTACAATCAACAGCTTGGAGGCTGAAGATGC
TGCCACTTATTACTGCCAACAGTGGAGTAGTAACCCGCTCA
CGTTCGGTGGCGGGACCAAGGTGGAGATCAAA

B) anti-CD3 (VH2/VL1)

DVQLVQSGAEVKKPGASVKVSCKASGYTATRYTMHWVRQAP
GQGLEWIGYINPSRGYTNIAQKLQGRVTMTTDTSTSTAYME
LSSLRSEDATYYCARYYDDHYCLDYWGQGTTVTVSSGEGT
STGSGGSGGSGGADDIQMTQSPSSLSASVGDRVITICRASQ
SVSYMNWYQQKPGKAPKRWIYDTSKVASGVPARFSGSGSGT
DYSLTINSLEAEDAATYYCQQWSSNPLTFGGGTKVEIK

Figure 3**C) anti-CD3 (VH2/VL2)**

GACGTCCAACCTGGTGCAGTCAGGGGGCTGAAGTGAAAAAACC
TGGGGCCTCAGTGAAGGTGTCCTGCAAGGCTTCTGGCTACA
CCGCTACTAGGTACACGATGCACTGGGGTAAGGCAGGCACCT
GGACAGGGTCTGGAATGGATTGGATACATTAATCCTAGCCG
TGGTTATACTAATTACGCACAGAAGTTGCAGGGGCCGCGTCA
CAATGACTACAGACACTTCCACCAGCACAGCCTACATGGAA
CTGAGCAGCCTGCGTTCTGAGGACACTGCAACCTATTACTG
TGCAAGATATTATGATGATCATTACTGCCTTGACTACTGGG
GCCAAGGCACCACGGTCACCGTCTCCTCAGGCGAAGGTACT
AGTACTGGTTCTGGTGGAAAGTGGAGGTTTCAGGTGGAGCAGA
CGACATTGTACTGACCCAGTCTCCAGCAACTCTGTCTCTGT
CTCCAGGGGGAGCGTGCCACCCTGAGCTGCAGAGCCAGTCAA
AGTGTAAGTTACATGAACTGGTACCAGCAGAAGCCGGGCAA
GGCACCCAAAAGATGGATTTATGACACATCCAAAGTGGCTT
CTGGAGTCCCTGCTCGCTTCAGTGGCAGTGGGTCTGGGACC
GACTACTCTCTCACAAATCAACAGCTTGGAGGCTGAAGATGC
TGCCACTTATTACTGCCAACAGTGGAGTAGTAACCCGCTCA
CGTTCGGTGGCGGGACCAAGGTGGAGATCAAA

D) anti-CD3 (VH2/VL2)

DVQLVQSGAEVKKPGASVKVSCKASGYTATRYTMHWVRQAP
GQGLEWIGYINPSRGYTNYAQKLQGRVTMTTDTSTSTAYME
LSSLRSEDATYYCARYYDDHYCLDYWGQGTTVTVSSGEGT
STGSGGSGGSGGADDIVLTQSPATLSLSPGERATLSCRASQ
SVSYMNWYQQKPGKAPKRWIYDTSKVASGVPARFSGSGSGT
DYSLTINSLEAEDAATYYCQQWSSNPLTFGGGGTKVEIK

Figure 3**E) anti-CD3 (VH2/VL3)**

GACGTCCAACCTGGTGCAGTCAGGGGCTGAAGTGAAAAAACC
TGGGGCCTCAGTGAAGGTGTCCTGCAAGGCTTCTGGCTACA
CCGCTACTAGGTACACGATGCACTGGGTAAGGCAGGCACCT
GGACAGGGTCTGGAATGGATTGGATACATTAATCCTAGCCG
TGGTTATACTAATTACGCACAGAAGTTGCAGGGGCCGCGTCA
CAATGACTACAGACACTTCCACCAGCACAGCCTACATGGAA
CTGAGCAGCCTGCGTTCTGAGGACACTGCAACCTATTACTG
TGCAAGATATTATGATGATCATTACTGCCTTGACTACTGGG
GCCAAGGCACCACGGTCACCGTCTCCTCAGGCGAAGGTACT
AGTACTGGTTCTGGTGGAAAGTGGAGGTTTCAGGTGGAGCAGA
CGACATTGTACTGACCCAGTCTCCAGCAACTCTGTCTCTGT
CTCCAGGGGGAGCGTGCCACCCTGACCTGCAGAGCCAGTTCA
AGTGTAAGTTACATGAACTGGTACCAGCAGAAGCCGGGGCAA
GGCACCCAAAAGATGGATTTATGACACATCCAAAGTGGCTT
CTGGAGTCCCTGCTCGCTTCAGTGGCAGTGGGTCTGGGACC
GACTACTCTCTCACAATCAACAGCTTGGAGGCTGAAGATGC
TGCCACTTATTACTGCCAACAGTGGAGTAGTAACCCGCTCA
CGTTCGGTGGCGGGACCAAGGTGGAGATCAAA

F) anti-CD3 (VH2/VL3)

DVQLVQSGAEVKKPGASVKVSCKASGYTATRYTMHWVRQAP
GQGLEWIGYINPSRGYTNYAQKLQGRVTMTTDTSTSTAYME
LSSLRSEDATYYCARYYDDHYCLDYWGQGTTVTVSSGEGT
STGSGGSGGSGGADDIVLTQSPATLSLSPGERATLTCRASS
SVSYMNWYQQKPGKAPKRWIYDTSKVASGVPARFSGSGSGT
DYSLTINSLEAEDAATYYCQQWSSNPLTFGGGTKVEIK

Figure 4**A) anti-CD3 (VH3/VL1)**

GACGTCCAACCTGGTGCAGTCAGGGGGCTGAAGTGAAAAAACC
TGGGGCCTCAGTGAAGGTGTCCTGCAAGGCTTCTGGCTACA
CCGCTACTAGGTACACGATGCACTGGGTAAGGCAGGCACCT
GGACAGGGTCTGGAATGGATTGGATACATTAATCCTAGCCG
TGGTTATACTAATTACGCACAGAAGTTGCAGGGGCCGCGTCA
CAATGACTACAGACACTTCCACCAGCACAGCCTACCTGCAA
ATGAACAGCCTGAAAACCTGAGGACACTGCAGTCTATTACTG
TGCAAGATATTATGATGATCATTACTGCCTTGACTACTGGG
GCCAAGGCACCACGGTCACCGTCTCCTCAGGCGAAGGTACT
AGTACTGGTTCTGGTGGAGGTGGAGGTTTCAGGTGGAGCAGA
CGACATTCAGATGACCCAGTCTCCATCTAGCCTGTCTGCAT
CTGTCGGGGACCGTGTCACCATCACCTGCAGAGCCAGTCAA
AGTGTAAGTTACATGAACTGGTACCAGCAGAAGCCGGGCAA
GGCACCCAAAAGATGGATTTATGACACATCCAAAGTGGCTT
CTGGAGTCCCTGCTCGCTTCAGTGGCAGTGGGTCTGGGACC
GACTACTCTCTCACAATCAACAGCTTGGAGGCTGAAGATGC
TGCCACTTATTACTGCCAACAGTGGAGTAGTAACCCGCTCA
CGTTCGGTGGCGGGACCAAGGTGGAGATCAAA

B) anti-CD3 (VH3/VL1)

DVQLVQSGAEVKKPGASVKVSCKASGYTATRYTMHWVRQAPGQ
GLEWIGYINPSRGYTNIAQKLQGRVTMTTDTSTSTAYLQMNSL
KTEDTAVYYCARYYDDHYCLDYWGQGTTVTVSSGEGTSTGSGG
SGGSGGADDIQMTQSPSSLSASVGDRVITCRASQSVSYMNWY
QQKPGKAPKRWIYDTSKVASGVPARFSGSGSGTDYSLTINSLE
AEDAATYYCQQWSSNPLTFGGGTKVEIK

Figure 4**C) anti-CD3 (VH3/VL2)**

GACGTCCAACCTGGTGCAGTCAGGGGCTGAAGTGAAAAAACC
TGGGGCCTCAGTGAAGGTGTCCTGCAAGGCTTCTGGCTACA
CCGCTACTAGGTACACGATGCACTGGGTAAGGCAGGCACCT
GGACAGGGTCTGGAATGGATTGGATACATTAATCCTAGCCG
TGGTTATACTAATTACGCACAGAAGTTGCAGGGCCGCGTCA
CAATGACTACAGACACTTCCACCAGCACAGCCTACCTGCAA
ATGAACAGCCTGAAAACCTGAGGACACTGCAGTCTATTACTG
TGCAAGATATTATGATGATCATTACTGCCTTGACTACTGGG
GCCAAGGCACCACGGTCACCGTCTCCTCAGGCGAAGGTACT
AGTACTGGTTCTGGTGGAAAGTGGAGGTTTCAGGTGGAGCAGA
CGACATTGTACTGACCCAGTCTCCAGCAACTCTGTCTCTGT
CTCCAGGGGAGCGTGCCACCCTGAGCTGCAGAGCCAGTCAA
AGTGTAAGTTACATGAACTGGTACCAGCAGAAGCCGGGCAA
GGCACCCAAAAGATGGATTTATGACACATCCAAAGTGGCTT
CTGGAGTCCCTGCTCGCTTCAGTGGCAGTGGGTCTGGGACC
GACTACTCTCTCACAATCAACAGCTTGGAGGCTGAAGATGC
TGCCACTTATTACTGCCAACAGTGGAGTAGTAACCCGCTCA
CGTTCGGTGGCGGGACCAAGGTGGAGATCAAA

D) anti-CD3 (VH3/VL2)

DVQLVQSGAEVKKPGASVKVSCKASGYTATRYTMHWVRQAP
GQGLEWIGYINPSRGYTNYAQKLQGRVTMTTDTSTSTAYLQ
MNSLKTEDTAVYYCARYYDDHYCLDYWGQGTTVTVSSGEGT
STGSGGSGGSGGADDIVLTQSPATLSLSPGERATLSCRASQ
SVSYMNWYQQKPGKAPKRWIYDTSKVASGVPARFSGSGSGT
DYSLTINSLEAEDAATYYCQQWSSNPLTFGGGTKVEIK

Figure 4**E) anti-CD3 (VH3/VL3)**

GACGTCCAACCTGGTGCAGTCAGGGGCTGAAGTGAAAAAACC
TGGGGCCTCAGTGAAGGTGTCCTGCAAGGCTTCTGGCTACA
CCGCTACTAGGTACACGATGCACTGGGTAAGGCAGGCACCT
GGACAGGGTCTGGAATGGATTGGATACATTAATCCTAGCCG
TGGTTATACTAATTACGCACAGAAGTTGCAGGGGCCGCGTCA
CAATGACTACAGACACTTCCACCAGCACAGCCTACCTGCAA
ATGAACAGCCTGAAAACCTGAGGACACTGCAGTCTATTACTG
TGCAAGATATTATGATGATCATTACTGCCTTGACTACTGGG
GCCAAGGCACCACGGTCACCGTCTCCTCAGGCGAAGGTACT
AGTACTGGTTCTGGTGGAAAGTGGAGGTTTCAGGTGGAGCAGA
CGACATTGTACTGACCCAGTCTCCAGCAACTCTGTCTCTGT
CTCCAGGGGGAGCGTGCCACCCTGACCTGCAGAGCCAGTTCA
AGTGTAAGTTACATGAACTGGTACCAGCAGAAGCCGGGCAA
GGCACCCAAAAGATGGATTTATGACACATCCAAAGTGGCTT
CTGGAGTCCCTGCTCGCTTCAGTGGCAGTGGGTCTGGGACC
GACTACTCTCTCACAATCAACAGCTTGGAGGCTGAAGATGC
TGCCACTTATTACTGCCAACAGTGGAGTAGTAACCCGCTCA
CGTTCGGTGGCGGGACCAAGGTGGAGATCAAA

F) anti-CD3 (VH3/VL3)

DVQLVQSGAEVKKPGASVKVSCKASGYTATRYTMHWVRQAP
GQGLEWIGYINPSRGYTNYAQKLQGRVTMTTDTSTSTAYLQ
MNSLKTEDTAVYYCARYYDDHYCLDYWGQGTTVTVSSGEGT
STGSGGSGGSGGADDIVLTQSPATLSLSPGERATLTCRASS
SVSYMNWYQQKPGKAPKRWIYDTSKVASGVPARFSGSGSGT
DYSLTINSLEAEDAATYYCQQWSSNPLTFGGGGTKVEIK

Figure 5**A) CD3 (VH5/VL1)**

GACGTCCAACCTGGTGCAGTCAGGGGGCTGAAGTGAAAAAACC
TGGGGCCTCAGTGAAGGTGTCCTGCAAGGCTTCTGGCTACA
CCTTTACTAGGTACACGATGCACTGGGTAAGGCAGGCACCT
GGACAGGGTCTGGAATGGATTGGATACATTAATCCTAGCCG
TGGTTATACTAATTACGCAGACAGCGTCAAGGGCCGCTTCA
CAATCACTACAGACAAATCCACCAGCACAGCCTACATGGAA
CTGAGCAGCCTGCGTTCTGAGGACACTGCAACCTATTACTG
TGCAAGATATTATGATGATCATTACTGCCTTGACTACTGGG
GCCAAGGCACCACGGTCACCGTCTCCTCAGGCGAAGGTACT
AGTACTGGTTCTGGTGGAAAGTGGAGGTTCAAGGTGGAGCAGA
CGACATTCAGATGACCCAGTCTCCATCTAGCCTGTCTGCAT
CTGTCGGGGACCGTGTCACCATCACCTGCAGAGCCAGTCAA
AGTGTAAGTTACATGAACTGGTACCAGCAGAAGCCGGGGCAA
GGCACCCAAAAGATGGATTTATGACACATCCAAAGTGGCTT
CTGGAGTCCCTGCTCGCTTCAGTGGCAGTGGGTCTGGGACC
GACTACTCTCTACAATCAACAGCTTGGAGGCTGAAGATGC
TGCCACTTATTACTGCCAACAGTGGAGTAGTAACCCGCTCA
CGTTCGGTGGCGGGACCAAGGTGGAGATCAAA

B) CD3 (VH5/VL1)

DVQLVQSGAEVKKPGASVKVSCKASGYTFTRYTMHWVRQAP
GQGLEWIGYINPSRGYTNADSVKGRFTITTDKSTSTAYME
LSSLRSEDATYYCARYYDDHYCLDYWGQGTTVTVSSGEGT
STGSGGSGGSGGADDIQMTQSPSSLSASVGDRVITCRASQ
SVSYMNWYQQKPGKAPKRWIYDTSKVASGVPARFSGSGSGT
DYSLTINSLEAEDAATYYCQQWSSNPLTFGGGTKVEIK

Figure 5**C) anti-CD3 (VH5/VL2)**

GACGTCCAACCTGGTGCAGTCAGGGGGCTGAAGTGAAAAAACC
TGGGGGCCTCAGTGAAGGTGTCCTGCAAGGCTTCTGGCTACA
CCTTTACTAGGTACACGATGCACTGGGTAAGGCAGGCACCT
GGACAGGGTCTGGAATGGATTGGATACATTAATCCTAGCCG
TGGTTATACTAATTACGCAGACAGCGTCAAGGGCCGCTTCA
CAATCACTACAGACAAATCCACCAGCACAGCCTACATGGAA
CTGAGCAGCCTGCGTTCTGAGGACACTGCAACCTATTACTG
TGCAAGATATTATGATGATCATTACTGCCTTGACTACTGGG
GCCAAGGCACCACGGTCACCGTCTCCTCAGGCGAAGGTACT
AGTACTGGTTCTGGTGGAAAGTGGAGGTTCAAGGTGGAGCAGA
CGACATTGTACTGACCCAGTCTCCAGCAACTCTGTCTCTGT
CTCCAGGGGGAGCGTGCCACCCTGAGCTGCAGAGCCAGTCAA
AGTGTAAGTTACATGAACTGGTACCAGCAGAAGCCGGGGCAA
GGCACCCAAAAGATGGATTTATGACACATCCAAAGTGGCTT
CTGGAGTCCCTGCTCGCTTCAGTGGCAGTGGGTCTGGGACC
GACTACTCTCTCACAATCAACAGCTTGGAGGCTGAAGATGC
TGCCACTTATTACTGCCAACAGTGGAGTAGTAACCCGCTCA
CGTTCGGTGGCGGGACCAAGGTGGAGATCAAA

D) anti-CD3 (VH5/VL2)

DVQLVQSGAEVKKPGASVKVSCKASGYTFTRYTMHWVRQAP
GQGLEWIGYINPSRGYTNADSVKGRFTITTDKSTSTAYME
LSSLRSEDATYYCARYYDDHYCLDYWGQGTTVTVSSGEGT
STGSGGSGGSGGADDIVLTQSPATLSLSPGERATLSCRASQ
SVSYMNWYQQKPGKAPKRWIYDTSKVASGVPARFSGSGSGT
DYSLTINSLEAEDAATYYCQQWSSNPLTFGGGGTKVEIK

Figure 5**E) anti-CD3 (VH5/VL3)**

GACGTCCAACCTGGTGCAGTCAGGGGGCTGAAGTGAAAAAACC
 TGGGGCCTCAGTGAAGGTGTCCTGCAAGGCTTCTGGCTACA
 CCTTTACTAGGTACACGATGCACTGGGTAAGGCAGGCACCT
 GGACAGGGTCTGGAATGGATTGGATACATTAATCCTAGCCG
 TGGTTATACTAATTACGCAGACAGCGTCAAGGGCCGCTTCA
 CAATCACTACAGACAAATCCACCAGCACAGCCTACATGGAA
 CTGAGCAGCCTGCGTTCTGAGGACACTGCAACCTATTACTG
 TGCAAGATATTATGATGATCATTACTGCCTTGACTACTGGG
 GCCAAGGCACCACGGTCACCGTCTCCTCAGGCGAAGGTACT
 AGTACTGGTTCTGGTGGGAAGTGGAGGTTTCAGGTGGAGCAGA
 CGACATTGTACTGACCCAGTCTCCAGCAACTCTGTCTCTGT
 CTCCAGGGGGAGCGTGCCACCCTGACCTGCAGAGCCAGTTCA
 AGTGTAAGTTACATGAACTGGTACCAGCAGAAGCCGGGCAA
 GGCACCCAAAAGATGGATTTATGACACATCCAAAGTGGCTT
 CTGGAGTCCCTGCTCGCTTCAGTGGCAGTGGGTCTGGGACC
 GACTACTCTCTCACAATCAACAGCTTGGAGGCTGAAGATGC
 TGCCACTTATTACTGCCAACAGTGGAGTAGTAACCCGCTCA
 CGTTCGGTGGCGGGACCAAGGTGGAGATCAAA

F) anti-CD3 (VH5/VL3)

DVQLVQSGAEVKKPGASVKVSCKASGYTFTRYTMHWVRQAP
 GQGLEWIGYINPSRGYTNADSVKGRFTITTDKSTSTAYME
 LSSLRSEDATYYCARYYDDHYCLDYWGQGTTVTVSSGEGT
 STGSGGSGGSGGADDIVLTQSPATLSLSPGERATLTCRASS
 SVSYMNWYQQKPGKAPKRWIYDTSKVASGVPARFSGSGSGT
 DYSLTINSLEAEDAATYYCQQWSSNPLTFGGGTKVEIK

Figure 6**A) anti-CD3 (VH7/VL1)**

GACGTCCAACCTGGTGCAGTCAGGGGGCTGAAGTGAAAAAACC
TGGGGCCTCAGTGAAGGTGTCCTGCAAGGCTTCTGGCTACA
CCTTTACTAGGTACACGATGCACTGGGTAAGGCAGGCACCT
GGACAGGGTCTGGAATGGATTGGATACATTAATCCTAGCCG
TGGTTATACTAATTACAATCAGAAGTTCAAGGACCGCGTCA
CAATCACTACAGACAAATCCACCAGCACAGCCTACATGGAA
CTGAGCAGCCTGCGTTCTGAGGACACTGCAGTCTATTACTG
TGCAAGATATTATGATGATCATTACTGCCTTGACTACTGGG
GCCAAGGCACCACGGTCACCGTCTCCTCAGGCGAAGGTACT
AGTACTGGTTCTGGTGGAAAGTGGAGGTTTCAGGTGGAGCAGA
CGACATTCAGATGACCCAGTCTCCATCTAGCCTGTCTGCAT
CTGTCGGGGACCGTGTCACCATCACCTGCAGAGCCAGTCAA
AGTGTAAGTTACATGAACTGGTACCAGCAGAAGCCGGGGCAA
GGCACCCAAAAGATGGATTTATGACACATCCAAAGTGGCTT
CTGGAGTCCCTGCTCGCTTCAGTGGCAGTGGGTCTGGGACC
GACTACTCTCTACAATCAACAGCTTGGAGGCTGAAGATGC
TGCCACTTATTACTGCCAACAGTGGAGTAGTAACCCGCTCA
CGTTCGGTGGCGGGACCAAGGTGGAGATCAAA

B) anti-CD3 (VH7/VL1)

DVQLVQSGAEVKKPGASVKVSCKASGYTFTRYTMHWVRQAP
GQGLEWIGYINPSRGYTNYNQKFKDRVTITTDKSTSTAYME
LSSLRSEDVAVYYCARYYDDHYCLDYWGQGTTVTVSSGEGT
STGSGGSGGSGGADDIQMTQSPSSLSASVGDRVTITCRASQ
SVSYMNWYQQKPGKAPKRWIYDTSKVASGVPAREFSGSGSGT
DYSLTINSLEAEDAATYYCQQWSSNPLTFGGGTKVEIK

Figure 6**C) anti-CD3 (VH7/VL2)**

GACGTCCAACCTGGTGCAGTCAGGGGCTGAAGTGAAAAAACC
TGGGGCCTCAGTGAAGGTGTCCTGCAAGGCTTCTGGCTACA
CCTTTACTAGGTACACGATGCACTGGGTAAGGCAGGCACCT
GGACAGGGTCTGGAATGGATTGGATACATTAATCCTAGCCG
TGGTTATACTAATTACAATCAGAAGTTCAAGGACCGCGTCA
CAATCACTACAGACAAATCCACCAGCACAGCCTACATGGAA
CTGAGCAGCCTGCGTTCTGAGGACACTGCAGTCTATTACTG
TGCAAGATATTATGATGATCATTACTGCCTTGACTACTGGG
GCCAAGGCACCACGGTCACCGTCTCCTCAGGCGAAGGTACT
AGTACTGGTTCTGGTGGAAAGTGGAGGTTTCAGGTGGAGCAGA
CGACATTGTACTGACCCAGTCTCCAGCAACTCTGTCTCTGT
CTCCAGGGGAGCGTGCCACCCTGAGCTGCAGAGCCAGTCAA
AGTGTAAGTTACATGAACTGGTACCAGCAGAAGCCGGGCAA
GGCACCCAAAAGATGGATTTATGACACATCCAAAGTGGCTT
CTGGAGTCCCTGCTCGCTTCAGTGGCAGTGGGTCTGGGACC
GACTACTCTCTCACAATCAACAGCTTGGAGGCTGAAGATGC
TGCCACTTATTACTGCCAACAGTGGAGTAGTAACCCGCTCA
CGTTCGGTGGCGGGACCAAGGTGGAGATCAAA

D) anti-CD3 (VH7/VL2)

DVQLVQSGAEVKKPGASVKVSCKASGYTFTRYTMHWVRQAP
GQGLEWIGYINPSRGYTNYNQKFKDRVITITDKSTSTAYME
LSSLRSEDVAVYYCARYYDDHYCLDYWGQGTTVTVSSGEGT
STGSGGSGGSGGADDIVLTQSPATLSLSPGERATLSCRASQ
SVSYMNWYQQKPGKAPKRWIYDTSKVASGVPAREFSGSGSGT
DYSLTINSLEAEDAATYYCQQWSSNPLTFGGGTKVEIK

Figure 6**E) anti-CD3 (VH7/VL3)**

GACGTCCAACCTGGTGCAGTCAGGGGCTGAAGTGAAAAAACC
TGGGGCCTCAGTGAAGGTGTCCTGCAAGGCTTCTGGCTACA
CCTTTACTAGGTACACGATGCACTGGGTAAGGCAGGCACCT
GGACAGGGTCTGGAATGGATTGGATACATTAATCCTAGCCG
TGGTTATACTAATTACAATCAGAAGTTCAAGGACCGCGTCA
CAATCACTACAGACAAATCCACCAGCACAGCCTACATGGAA
CTGAGCAGCCTGCGTTCTGAGGACACTGCAGTCTATTACTG
TGCAAGATATTATGATGATCATTACTGCCTTGACTACTGGG
GCCAAGGCACCACGGTCACCGTCTCCTCAGGCGAAGGTACT
AGTACTGGTTCTGGTGGAAAGTGGAGGTTCAAGGTGGAGCAGA
CGACATTGTACTGACCCAGTCTCCAGCAACTCTGTCTCTGT
CTCCAGGGGAGCGTGCCACCCTGACCTGCAGAGCCAGTTCA
AGTGTAAGTTACATGAACTGGTACCAGCAGAAGCCGGGCAA
GGCACCCAAAAGATGGATTTATGACACATCCAAAGTGGCTT
CTGGAGTCCCTGCTCGCTTCAGTGGCAGTGGGTCTGGGACC
GACTACTCTCTCACAAATCAACAGCTTGGAGGCTGAAGATGC
TGCCACTTATTACTGCCAACAGTGGAGTAGTAACCCGCTCA
CGTTCGGTGGCGGGACCAAGGTGGAGATCAAA

F) anti-CD3 (VH7/VL3)

DVQLVQSGAEVKKPGASVKVSCKASGYTFTRYTMHWVRQAP
GQGLEWIGYINPSRGYTNYNQKFKDRVITITDKSTSTAYME
LSSLRSEDVAVYYCARYYDDHYCLDYWGQGTTVTVSSEGT
STGSGGSGGSGGADDIVLTQSPATLSLSPGERATLTCRASS
SVSYMNWYQQKPGKAPKRWIYDTSKVASGVPAREFSGSGSGT
DYSLTINSLEAEDAATYYCQQWSSNPLTFGGGTKVEIK

Figure 7A

CD3 Binding Analysis

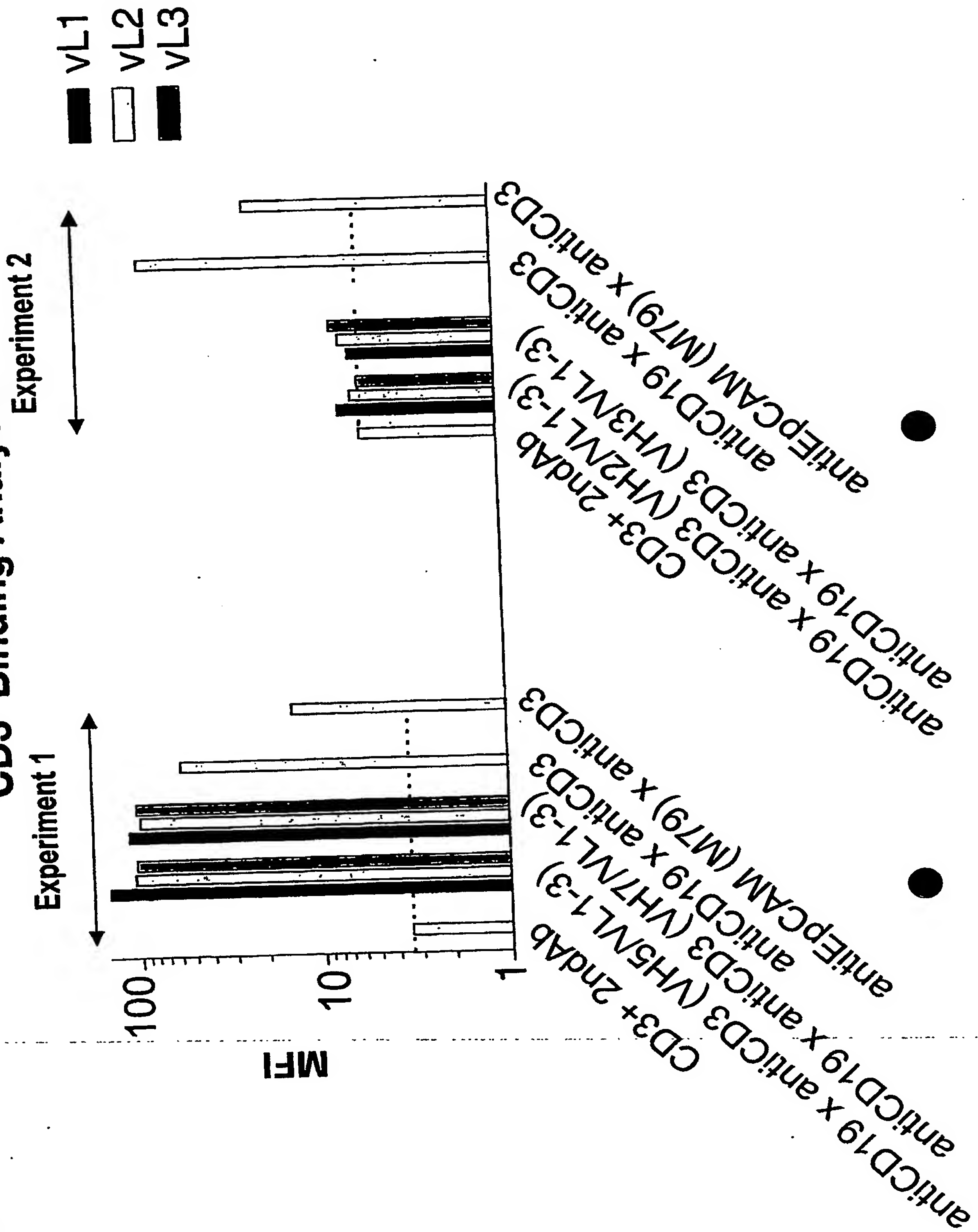


Figure 7B

CD19 Binding Analysis

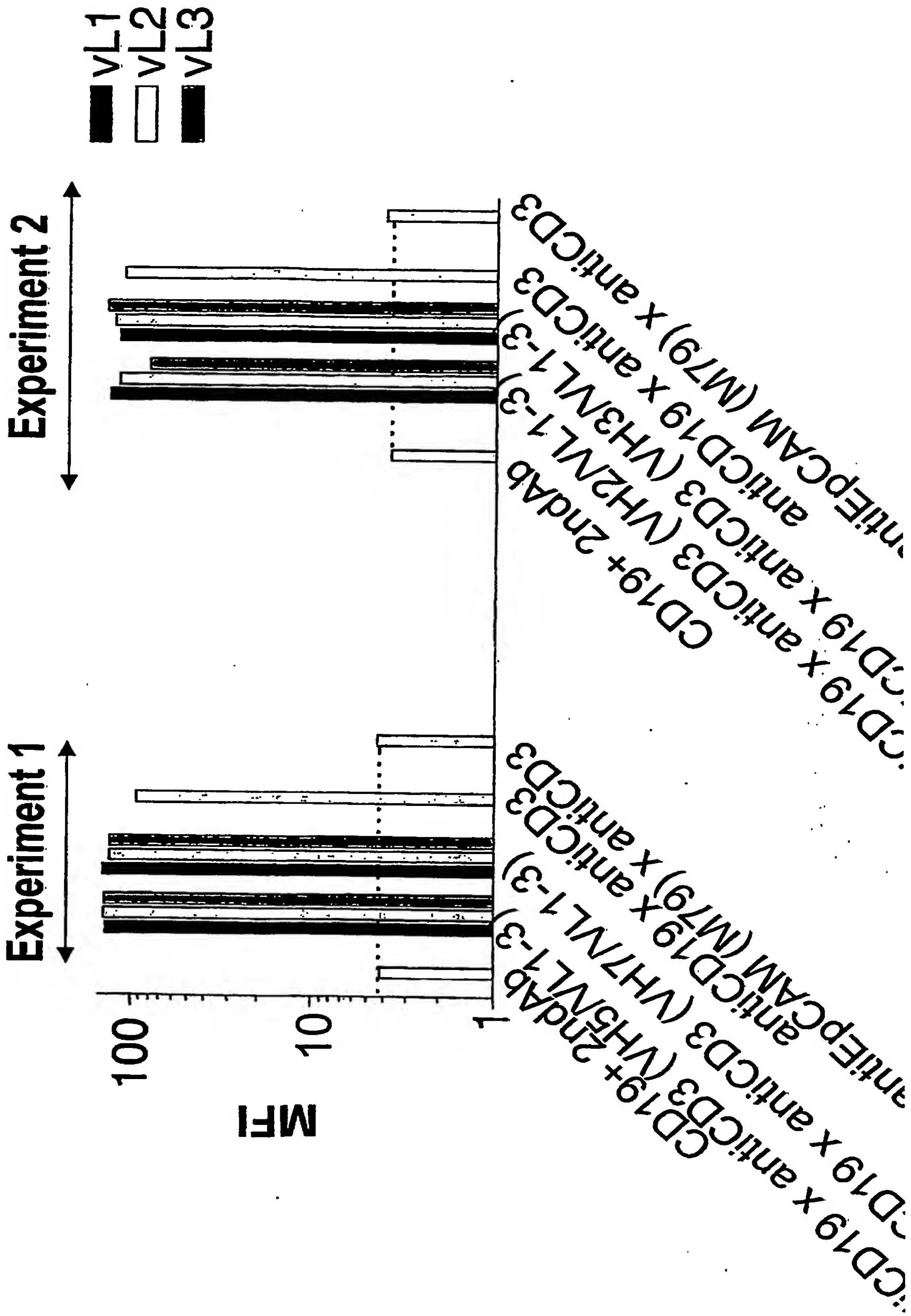
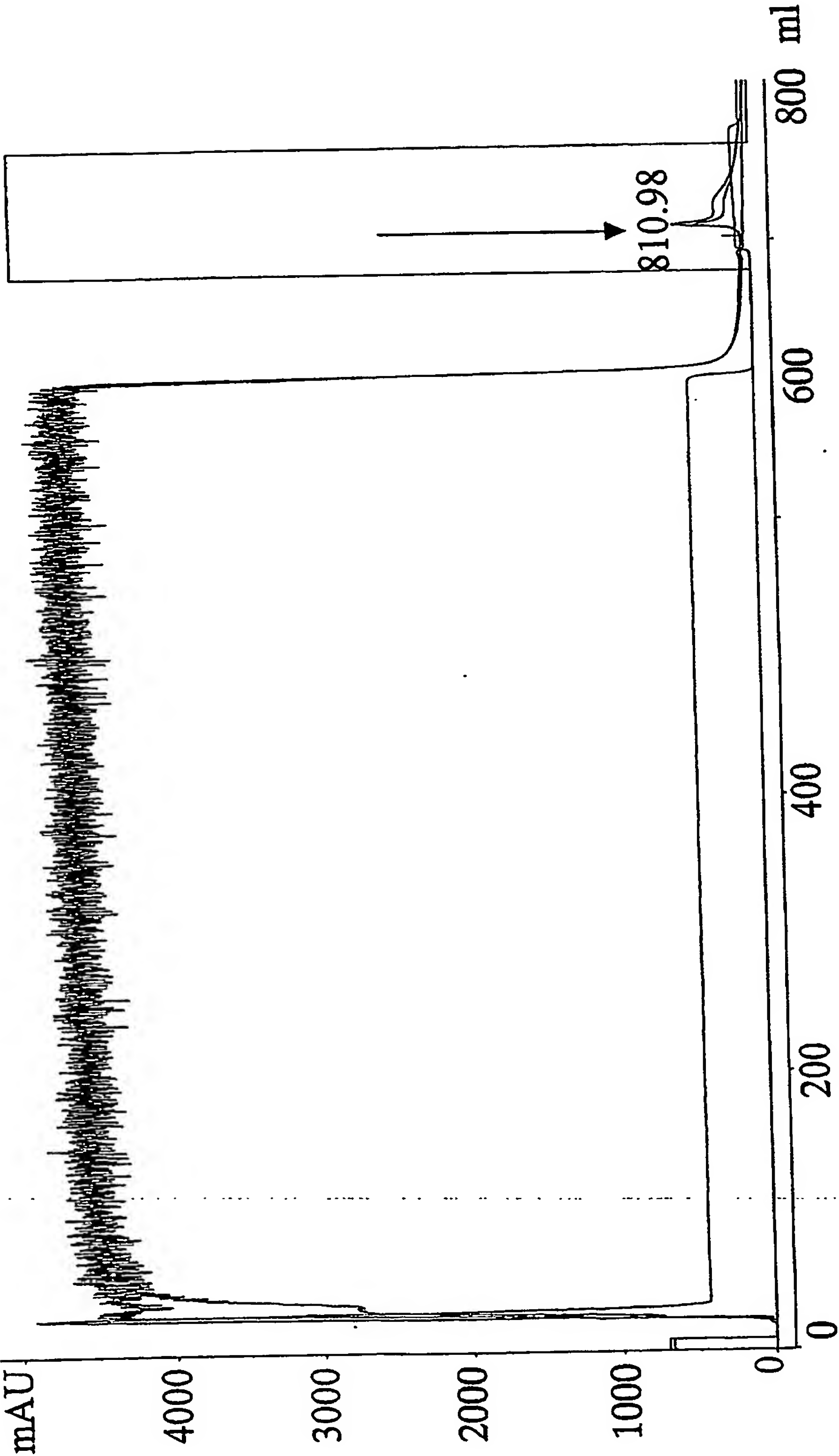


Figure 8



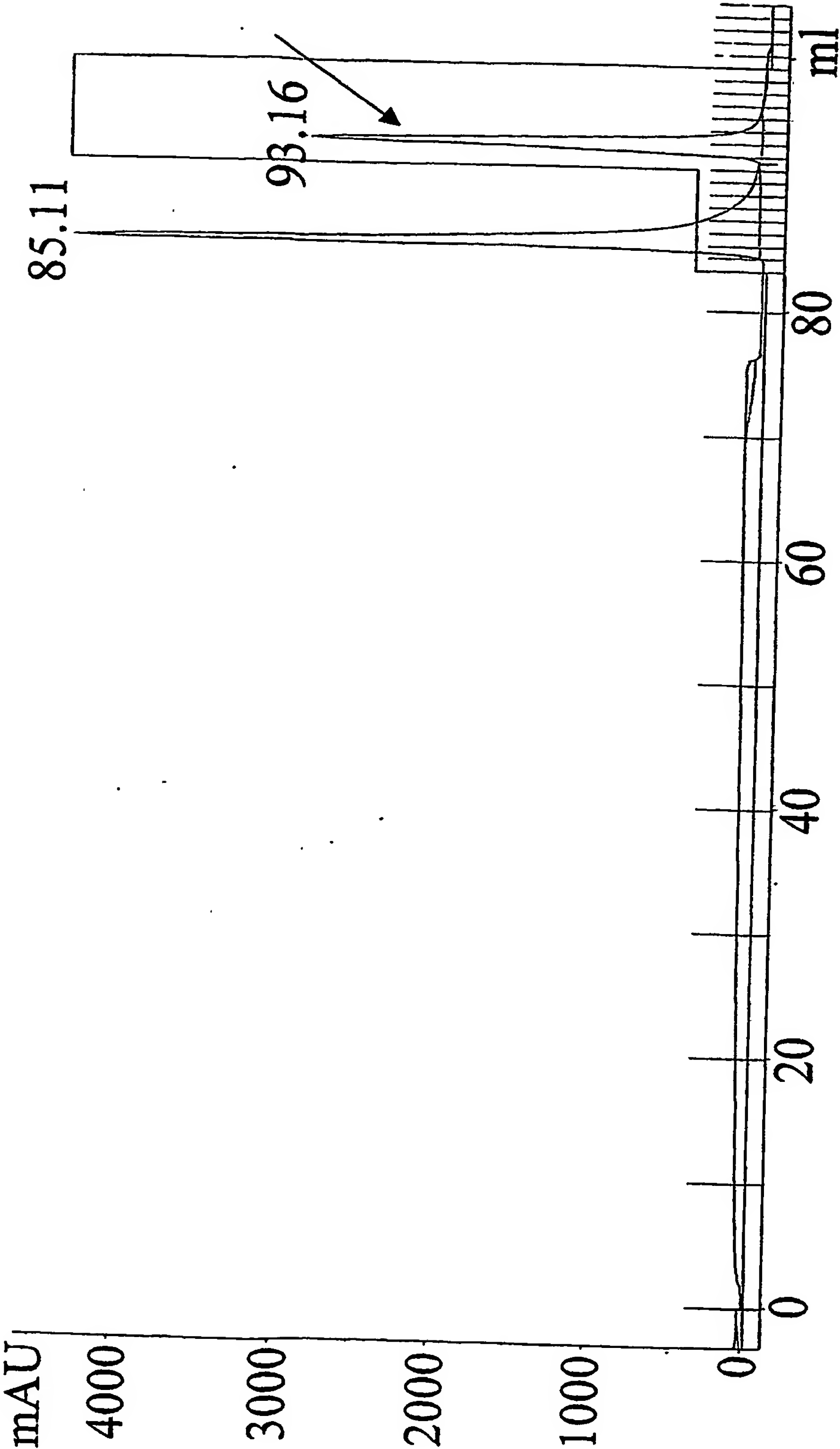


Figure 9

Figure 10

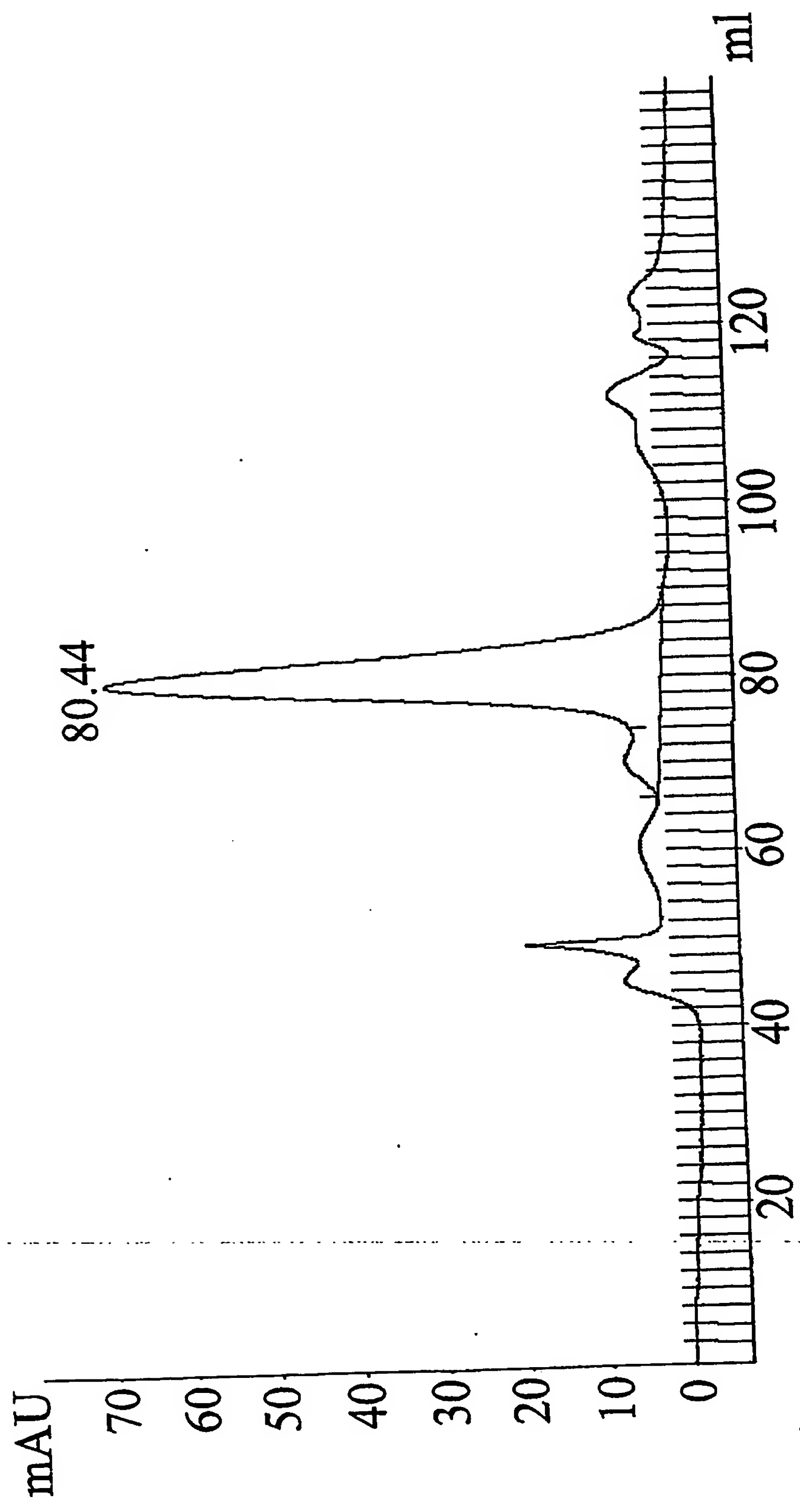
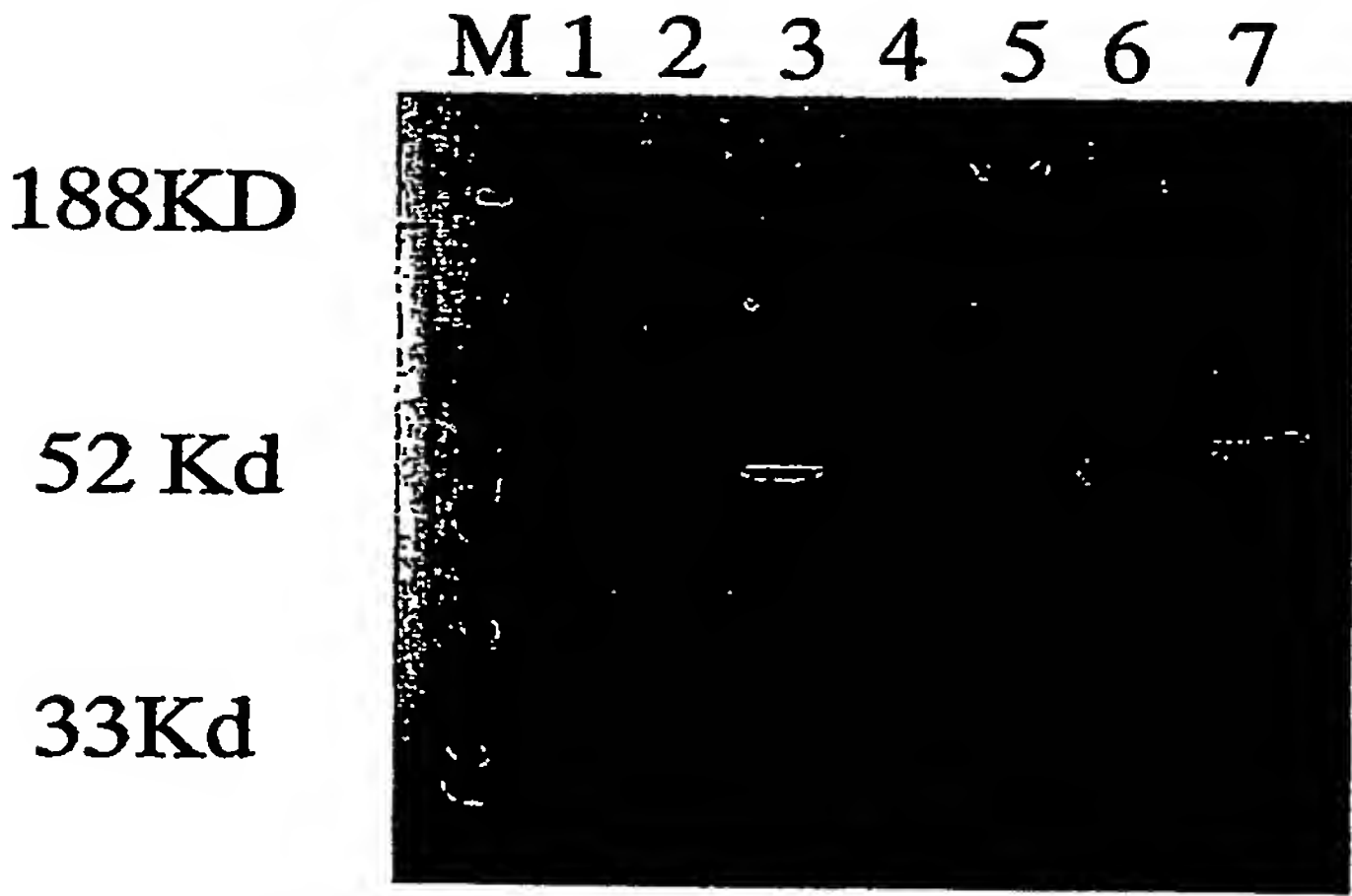


Figure 11

A)



B)

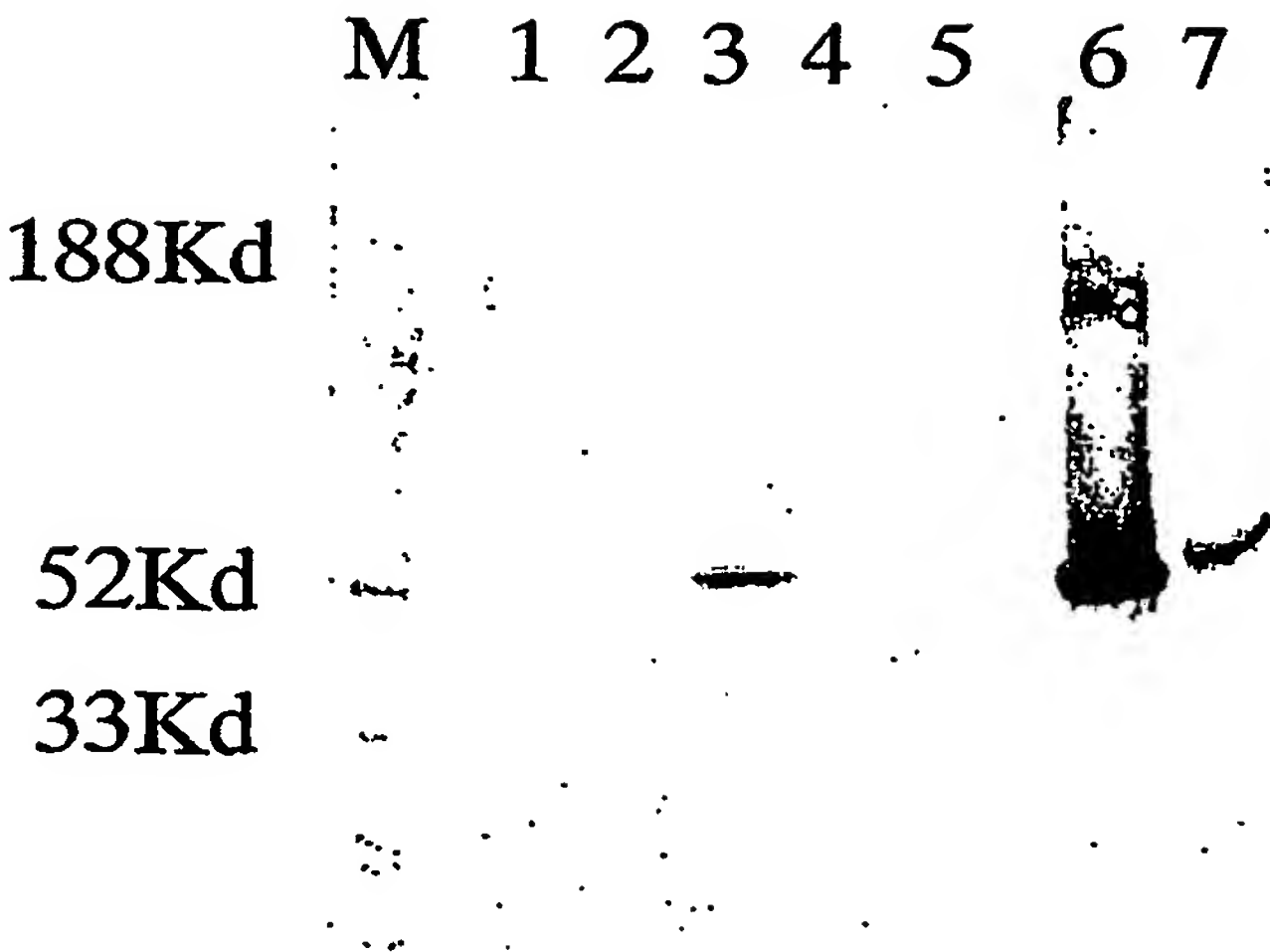


Figure 12A

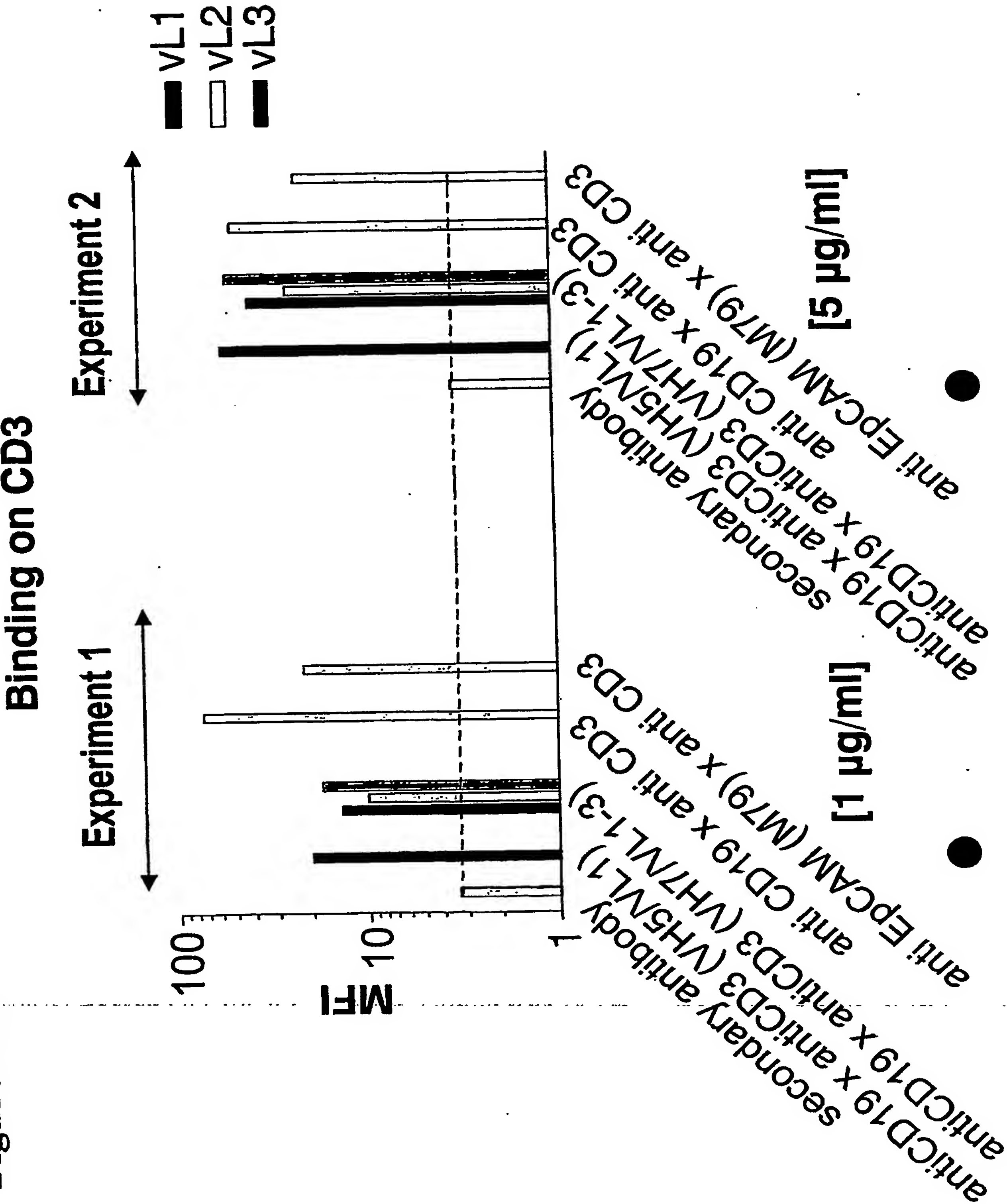


Figure 12B

Binding on CD19

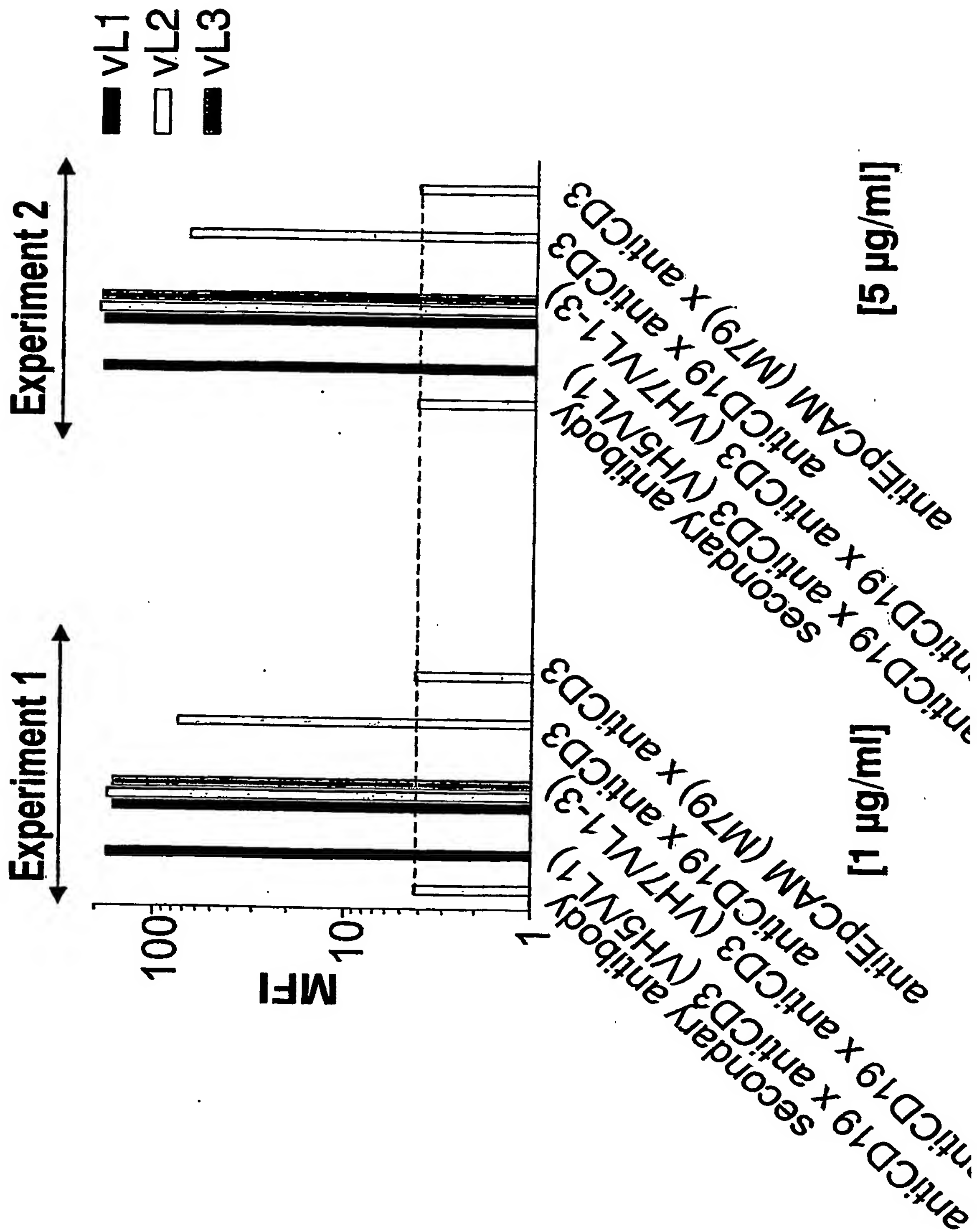


Figure 13

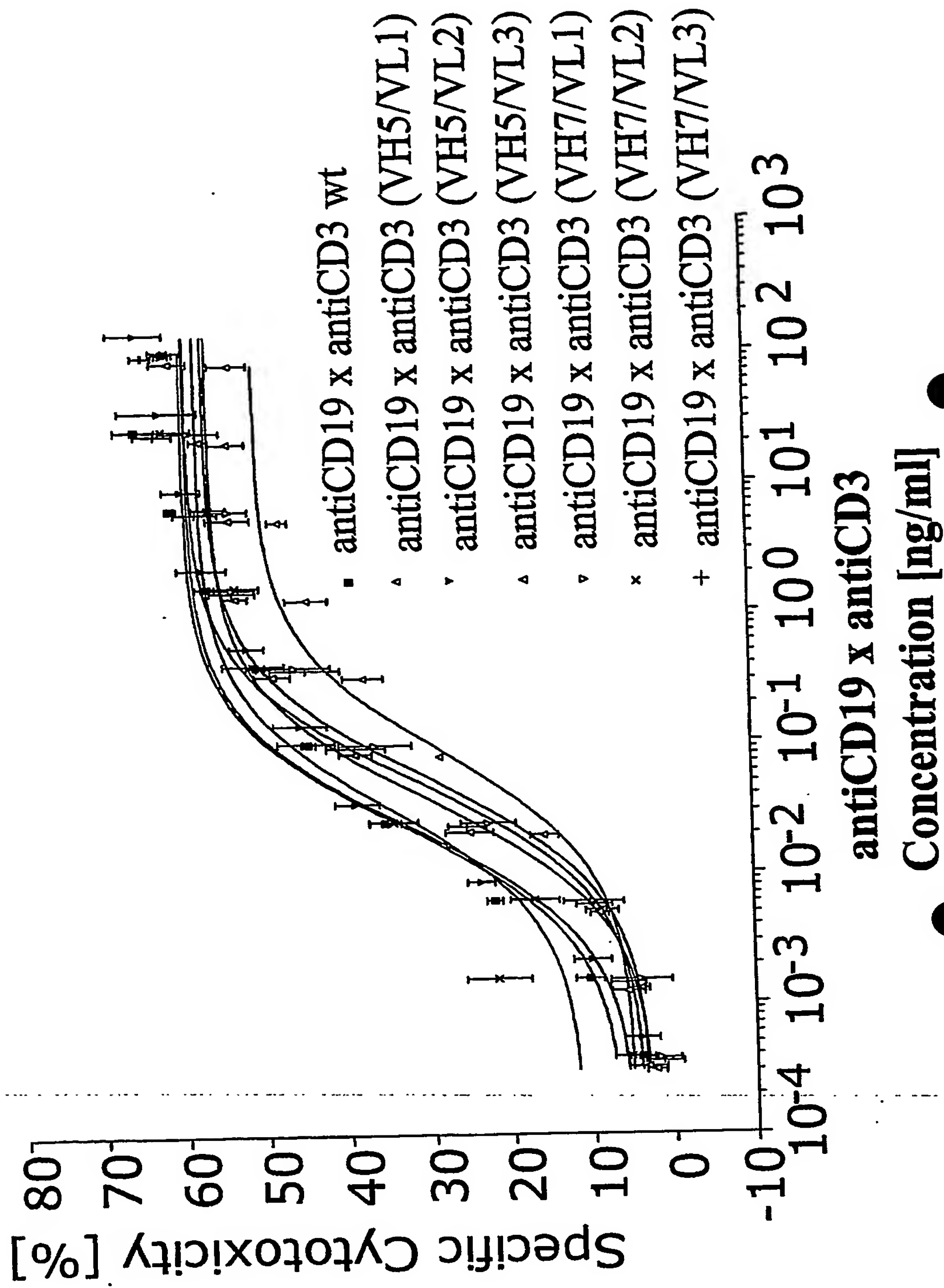


Figure 14

	FR1	CDR1	FR2	CDR2
nondeimmunized				
anti-CD3	DIKLQSGAELARPGASVKMSCKTSGYTF	TRYTMHWVKQRPQG	LEWIGYINPSRGYTNYNQKFKD	
anti-CD3 VH5	DVQLVQSGAEVKKPGASVKVSKKASGYTF	TRYTMHWVRQAPGQGLEWIGYINPSRGYTNADSVKG		
anti-CD3 VH7	DVQLVQSGAEVKKPGASVKVSKKASGYTF	TRYTMHWVRQAPGQGLEWIGYINPSRGYTNYNQKFKD		
anti-CD3 VH2	DVQLVQSGAEVKKPGASVKVSKKASGYTA	TRYTMHWVRQAPGQGLEWIGYINPSRGYTNQAQKLQG		
anti-CD3 VH3	DVQLVQSGAEVKKPGASVKVSKKASGYTA	TRYTMHWVRQAPGQGLEWIGYINPSRGYTNQAQKLQG		

	FR3	CDR3	FR4
nondeimmunized			
anti-CD3	KATLT	TDKSSSTAYMQLSSLTSEDS	AVYCARYYDDHYCLDYWGQGTTLTVSS
anti-CD3 VH5	RFTIT	TDKSTSTAYMELSSLRSEDT	ATYYCARYYDDHYCLDYWGQGTTLTVSS
anti-CD3 VH7	RVTIT	TDKSTSTAYMELSSLRSEDT	AVYCARYYDDHYCLDYWGQGTTLTVSS
anti-CD3 VH2	RVTMT	TDKSTSTAYMELSSLRSEDT	ATYYCARYYDDHYCLDYWGQGTTLTVSS
anti-CD3 VH3	RVTMT	TDKSTSTAYLQMNSLKTED	AVYCARYYDDHYCLDYWGQGTTLTVSS

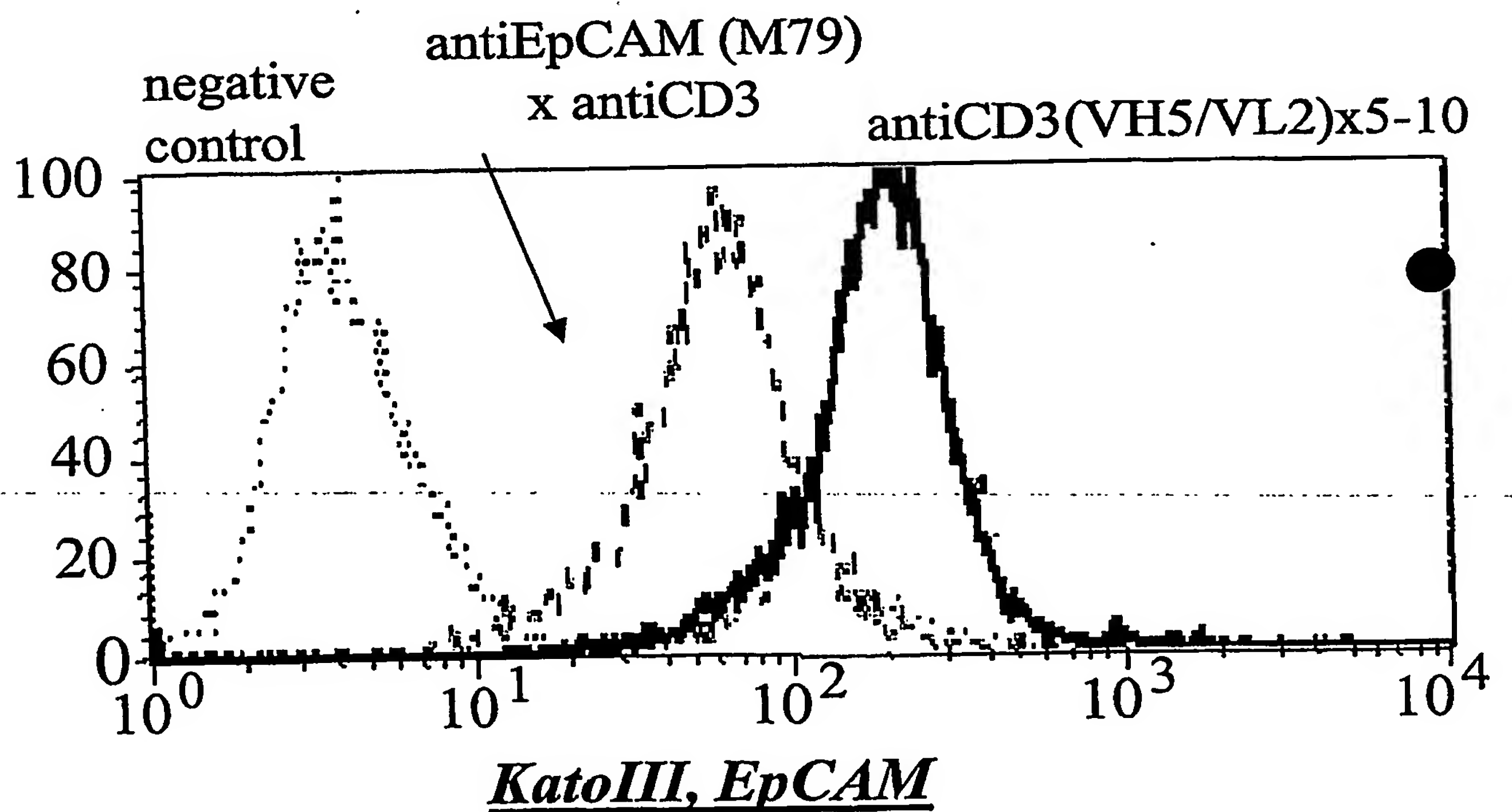
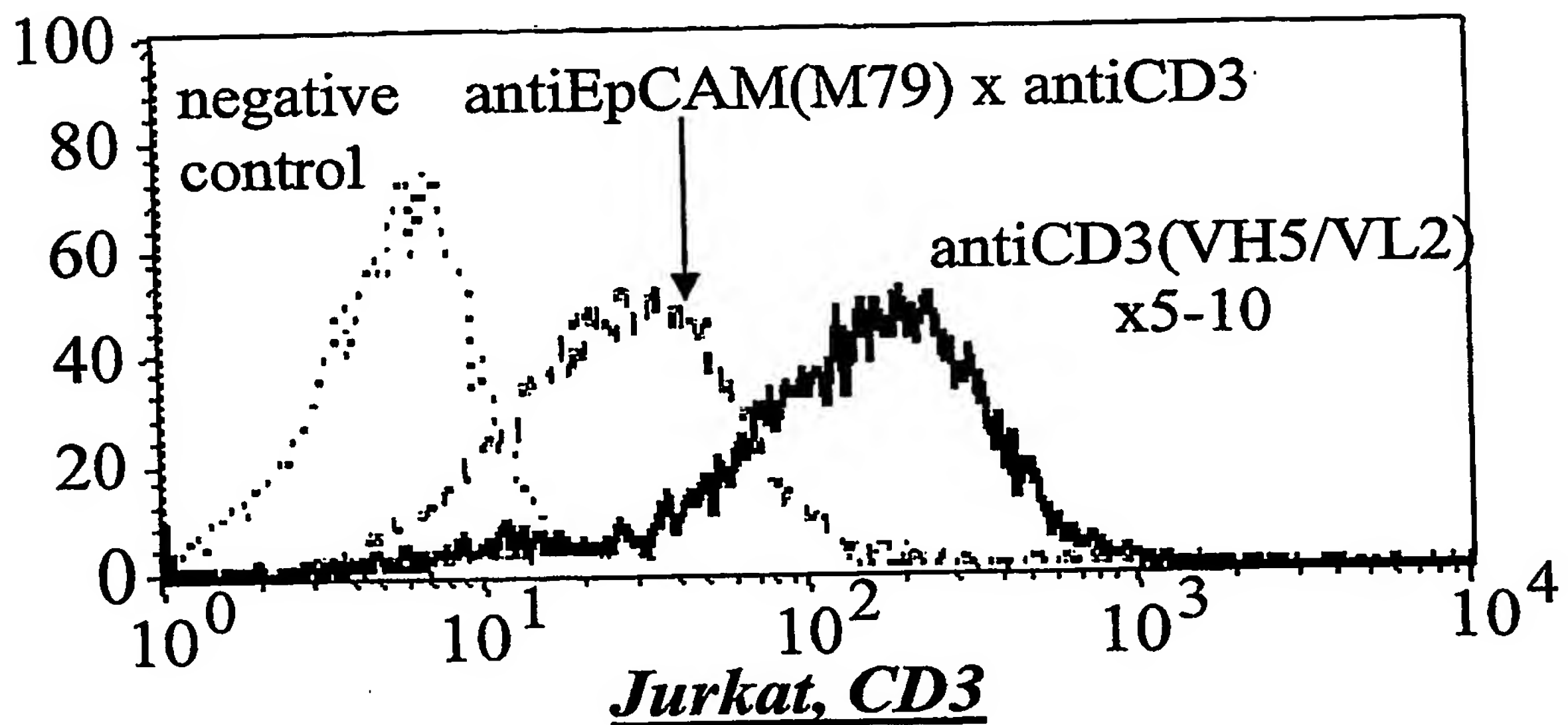
Figure 15 A**antiCD3(VH5/VL2) x 5-10 (SEQ ID NO: 37)**

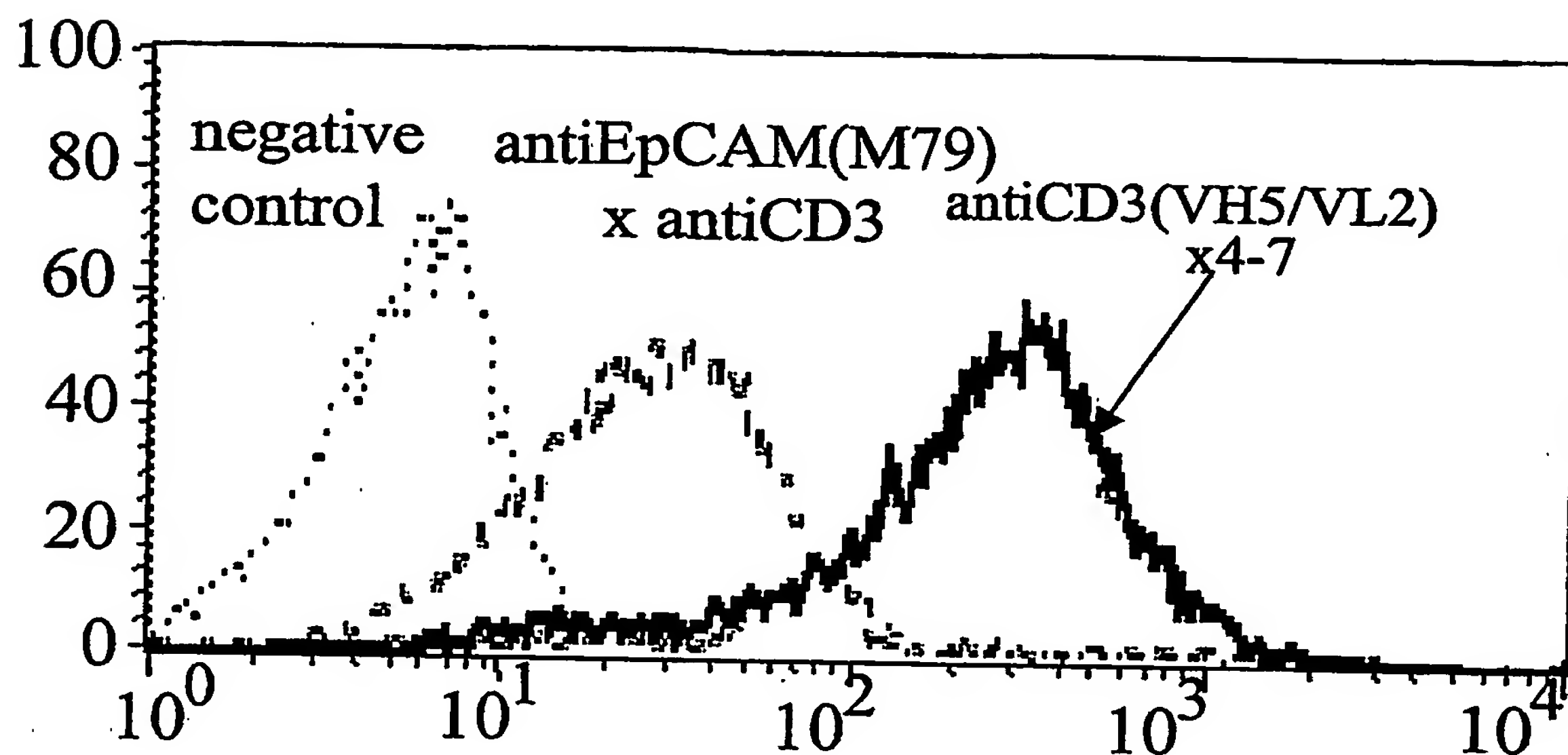
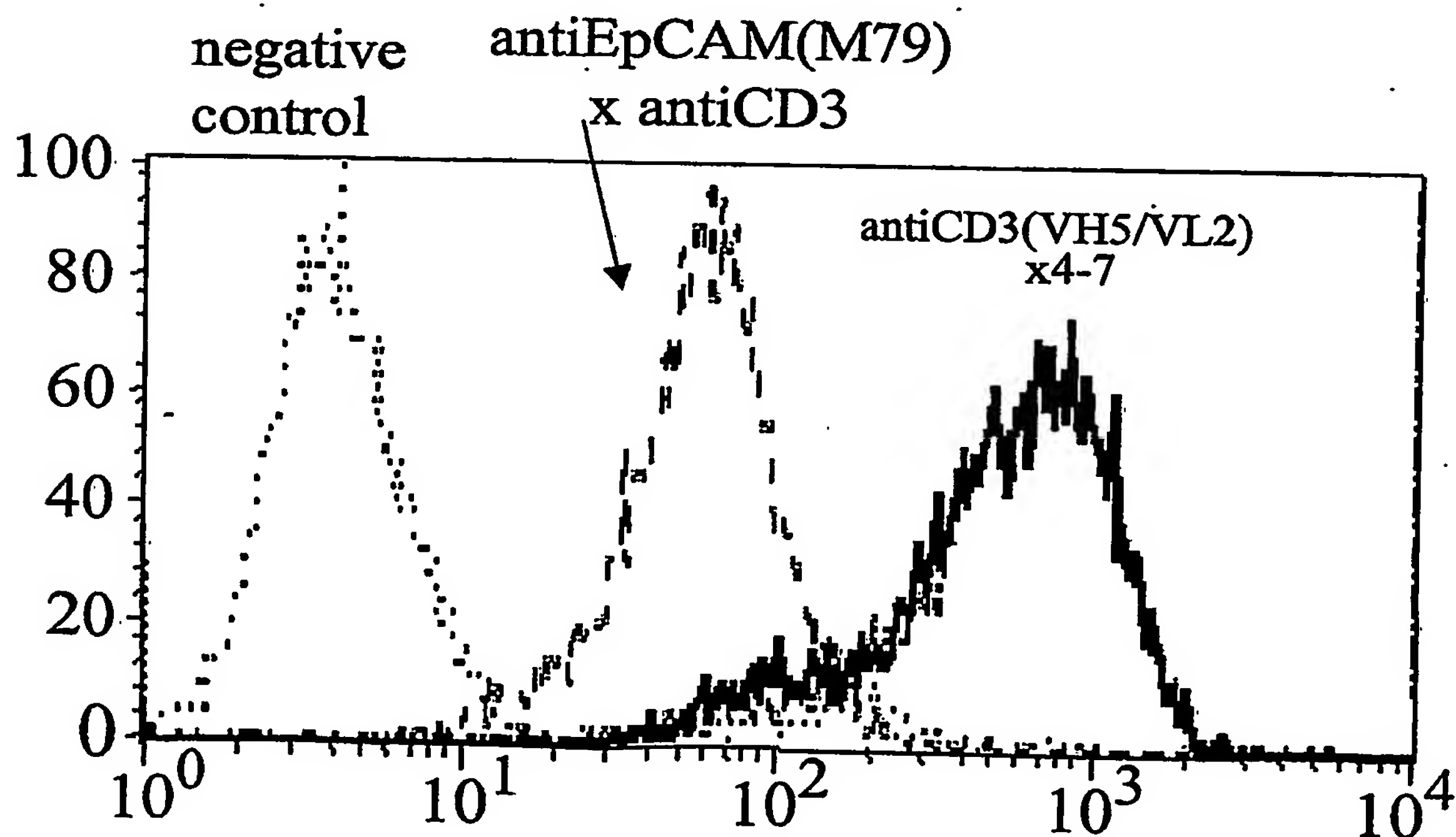
Figure 15B**antiCD3(VH5/VL2) x 4-7 (SEQ ID NO:33)****Jurkat, CD3****KatoIII, EpCAM**

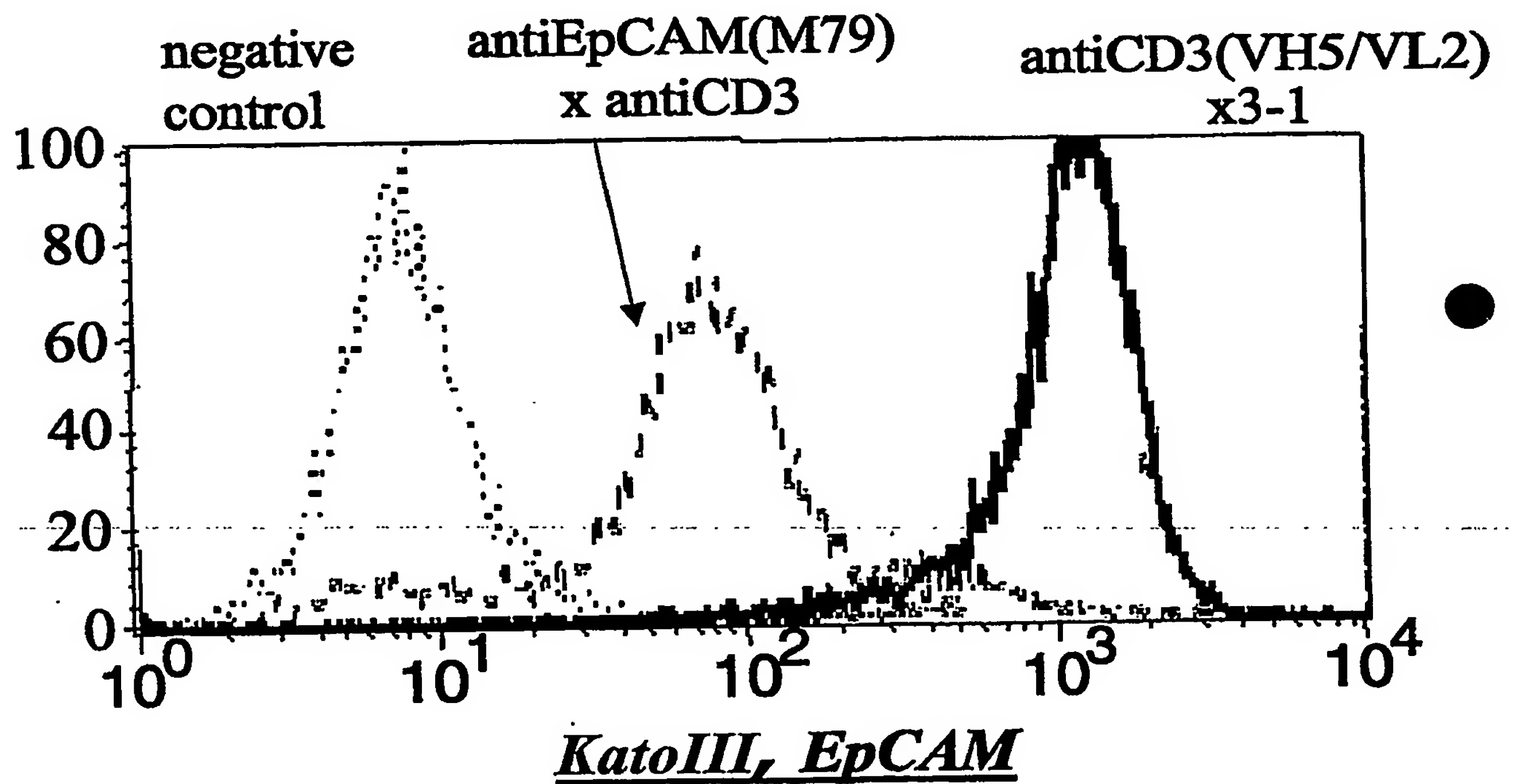
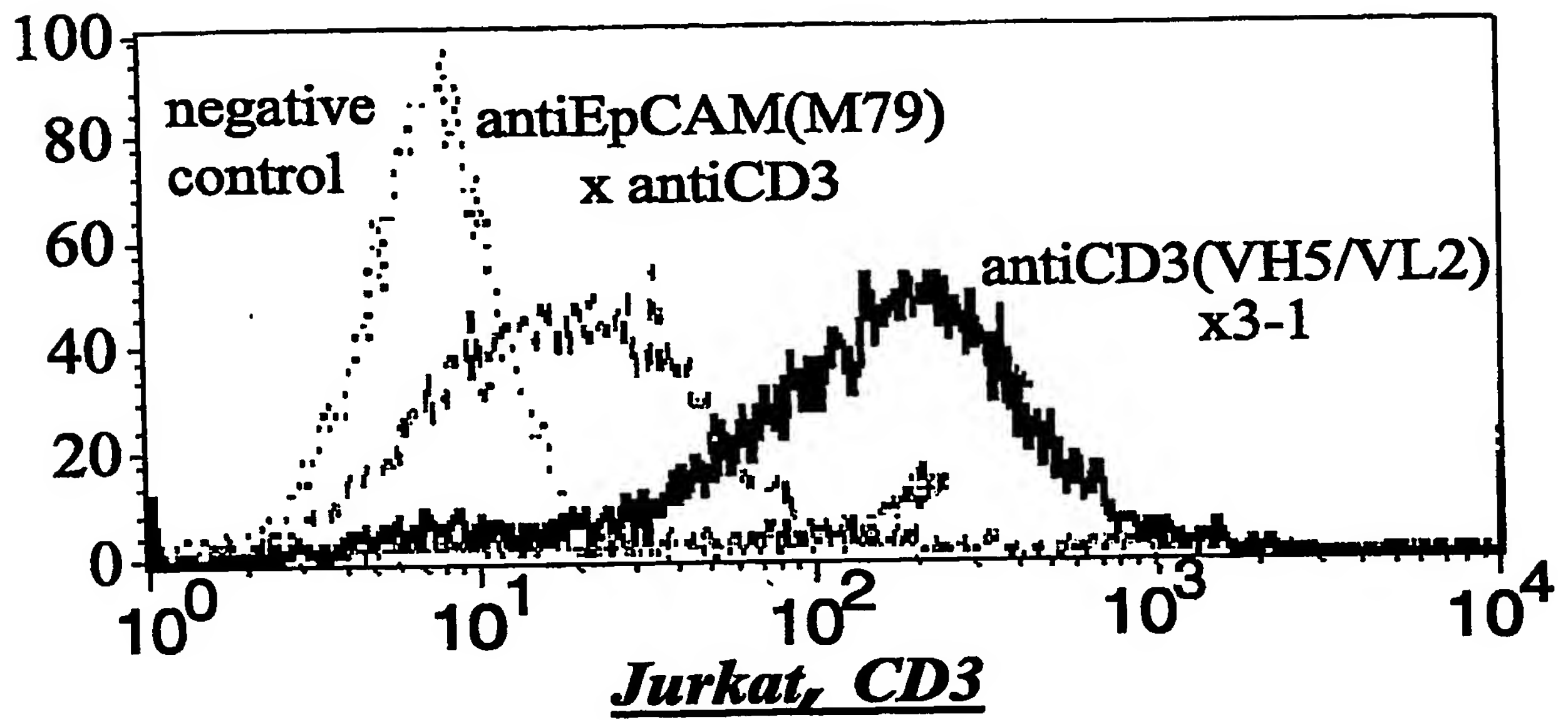
Figure 15C**antiCD3(VH5/VL2) x 3-1 (SEQ ID NO:31)**

Figure 15 D

**antiCD3(VH5/VL2) x 4-7 VL-VH
(SEQ ID NO: 35)**

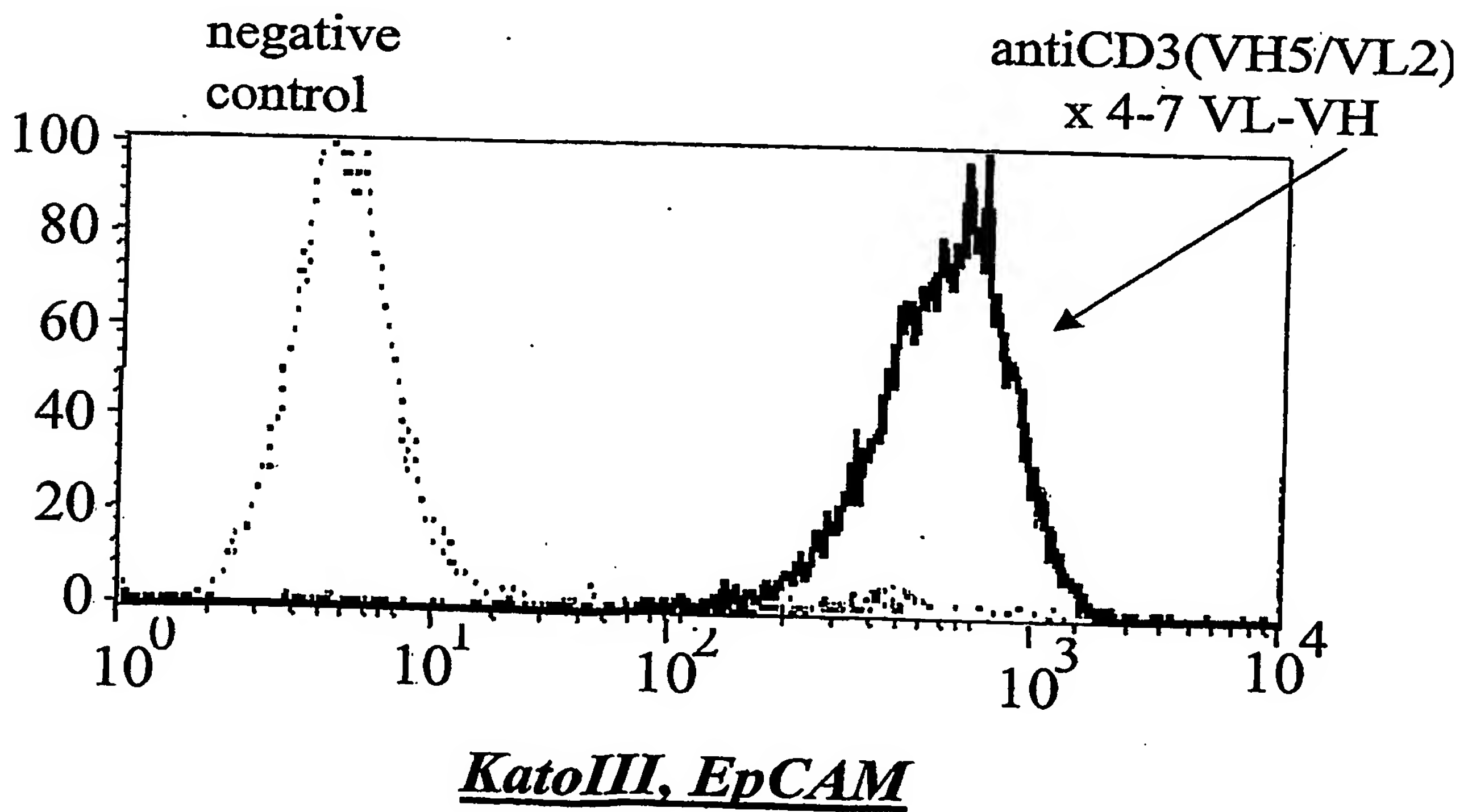
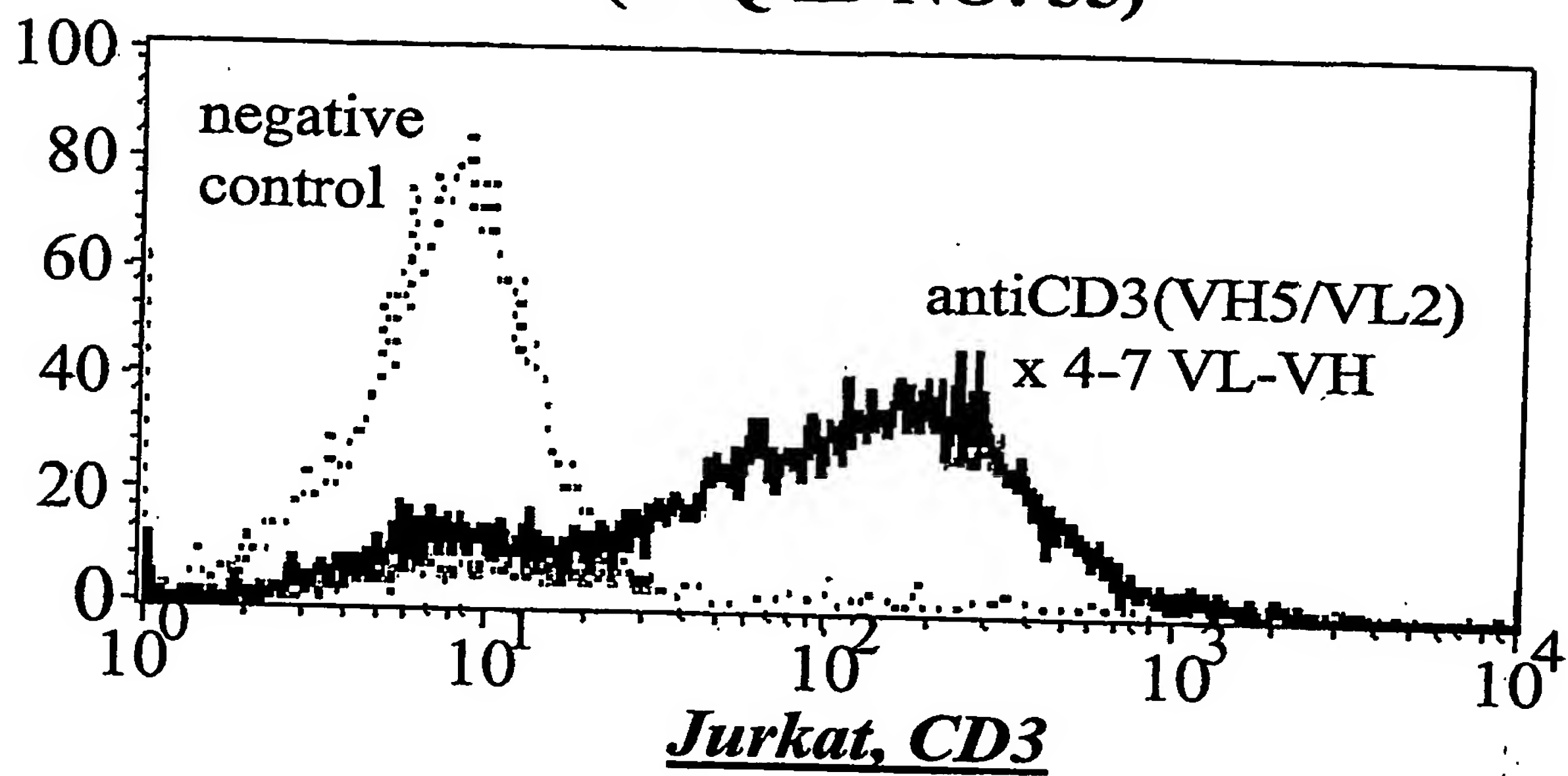


Figure 15 E

**antiCD3(VH5/VL2) x 5-10 VL-VH
(SEQ ID NO:39)**

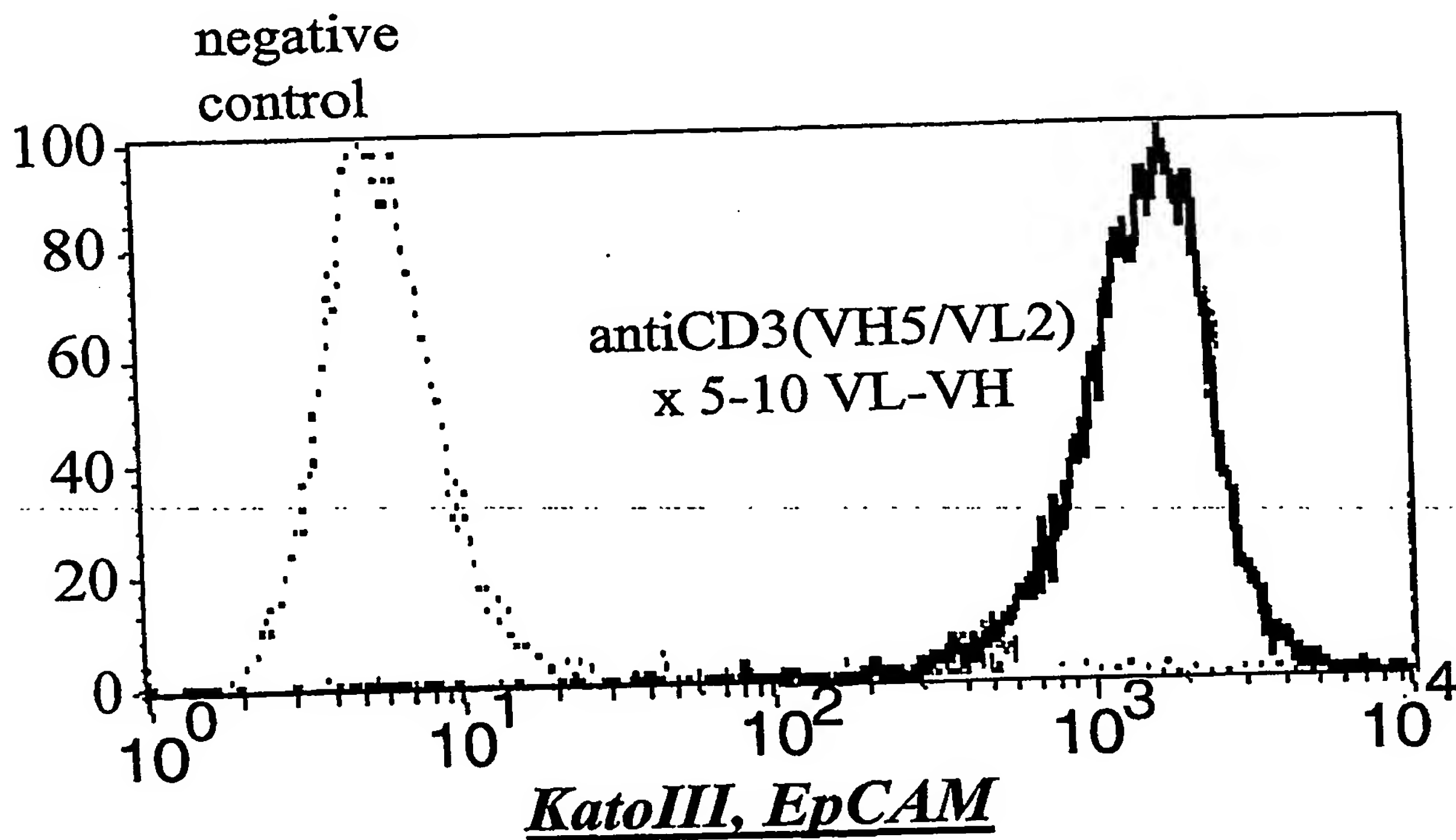
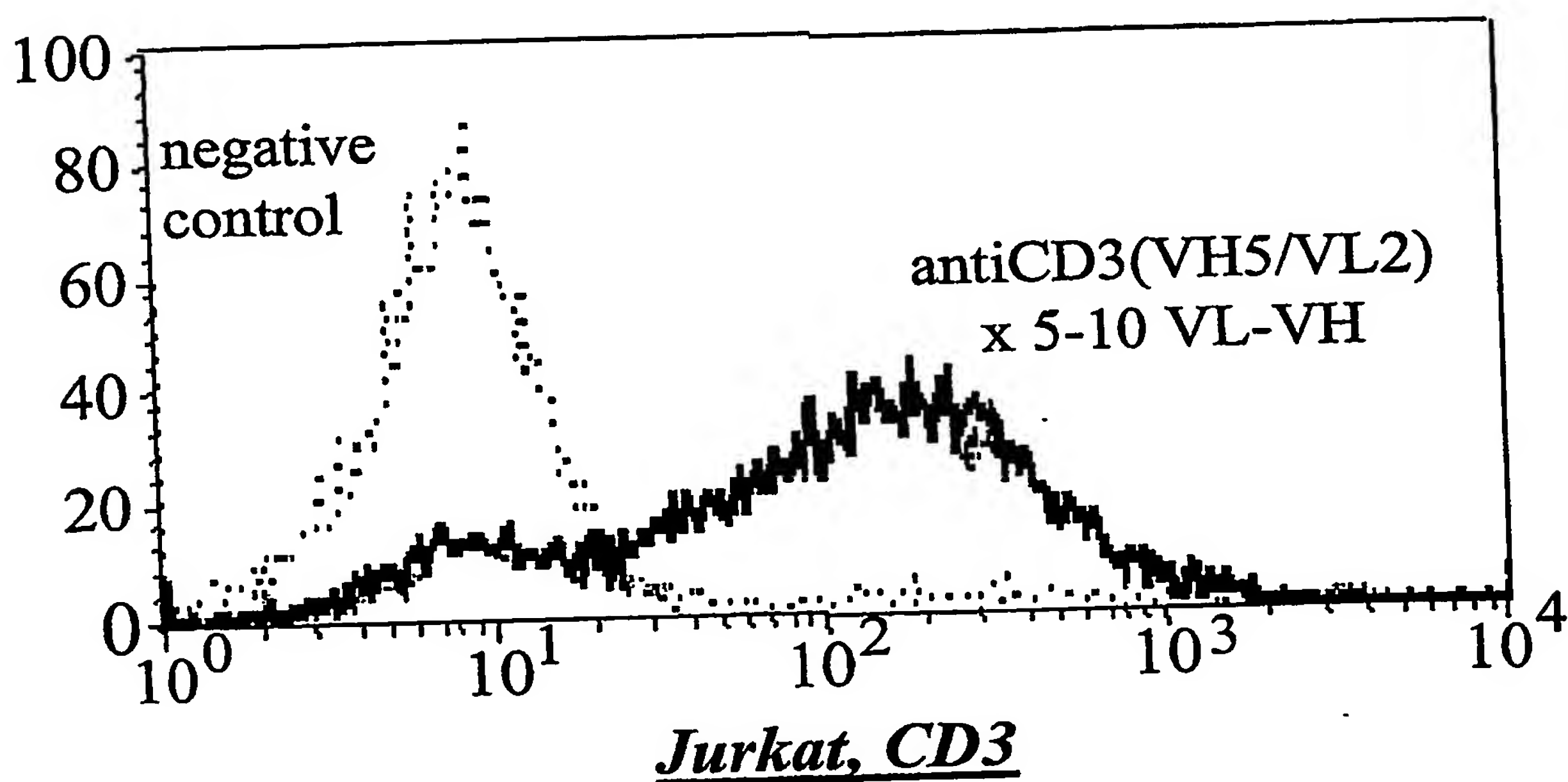
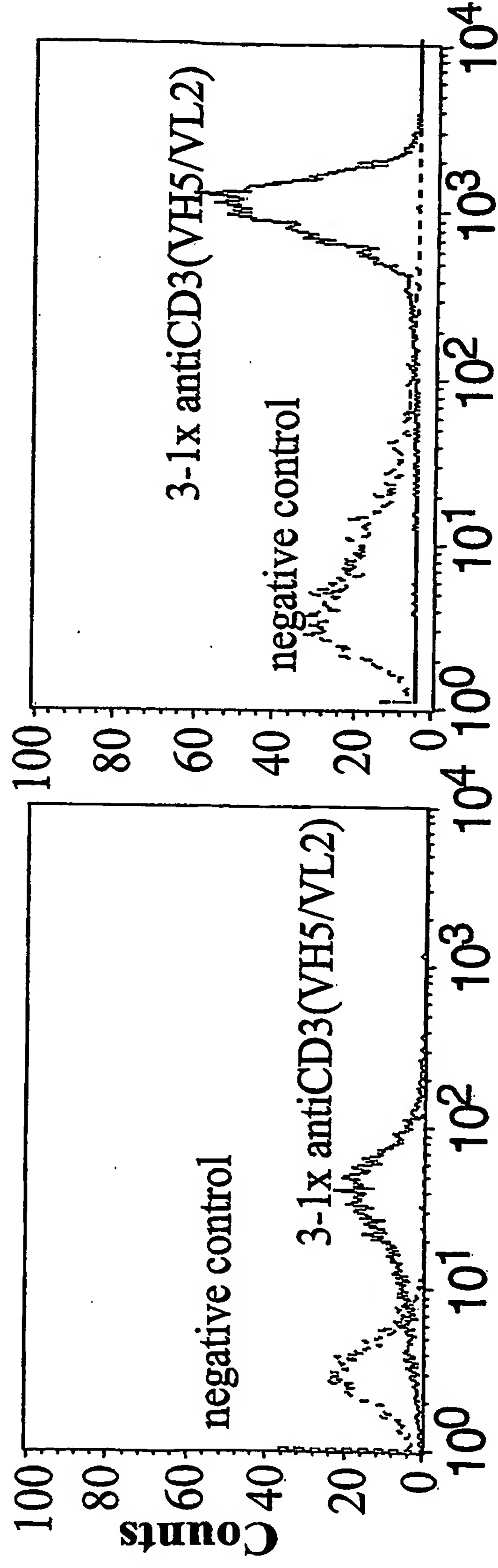


Figure 16 A

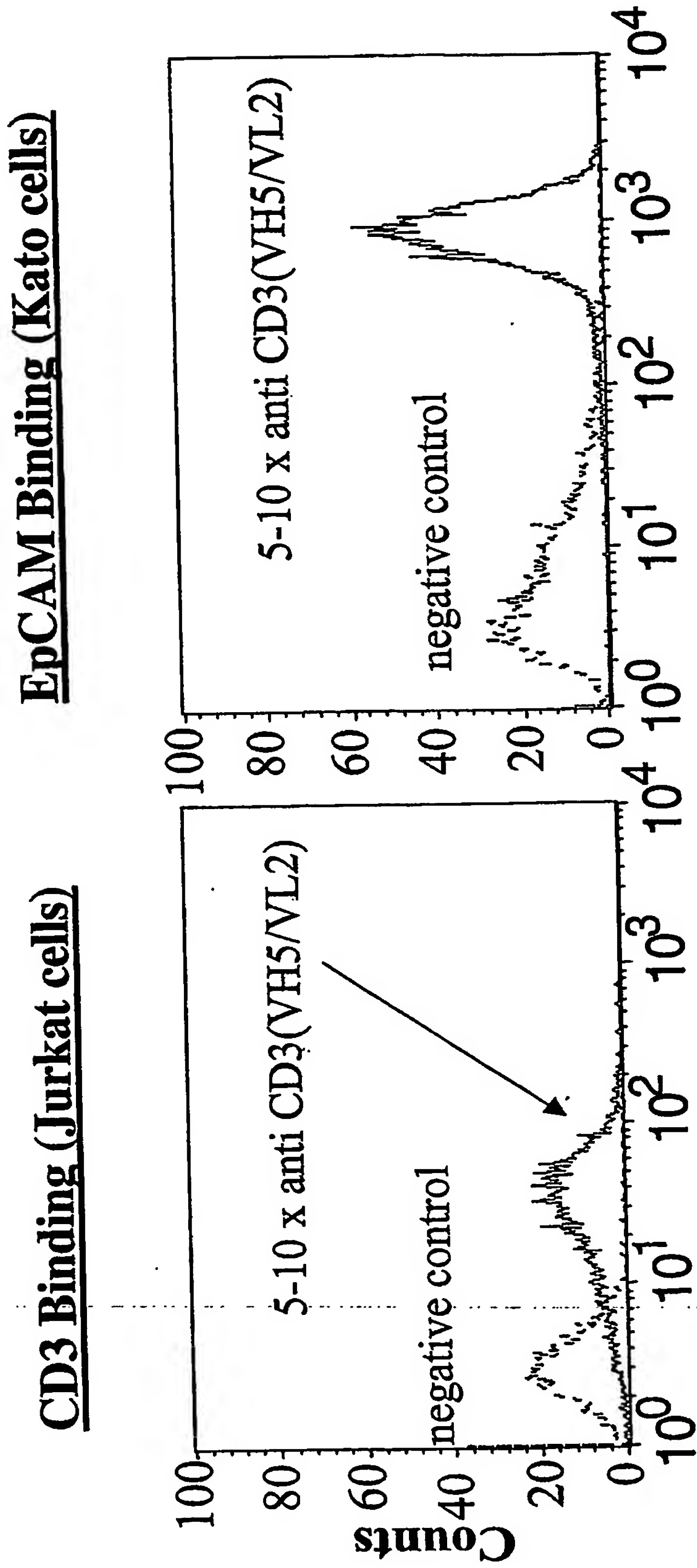
CD3 Binding (Jurkat cells)

EpCAM Binding (Kato cells)



3-1 x
antiCD3(VH5/VL2)
(SEQ ID NO: 49)

Figure 16 B



5-10 x antiCD3(VH5/VL2)

(SEQ ID NO:63)

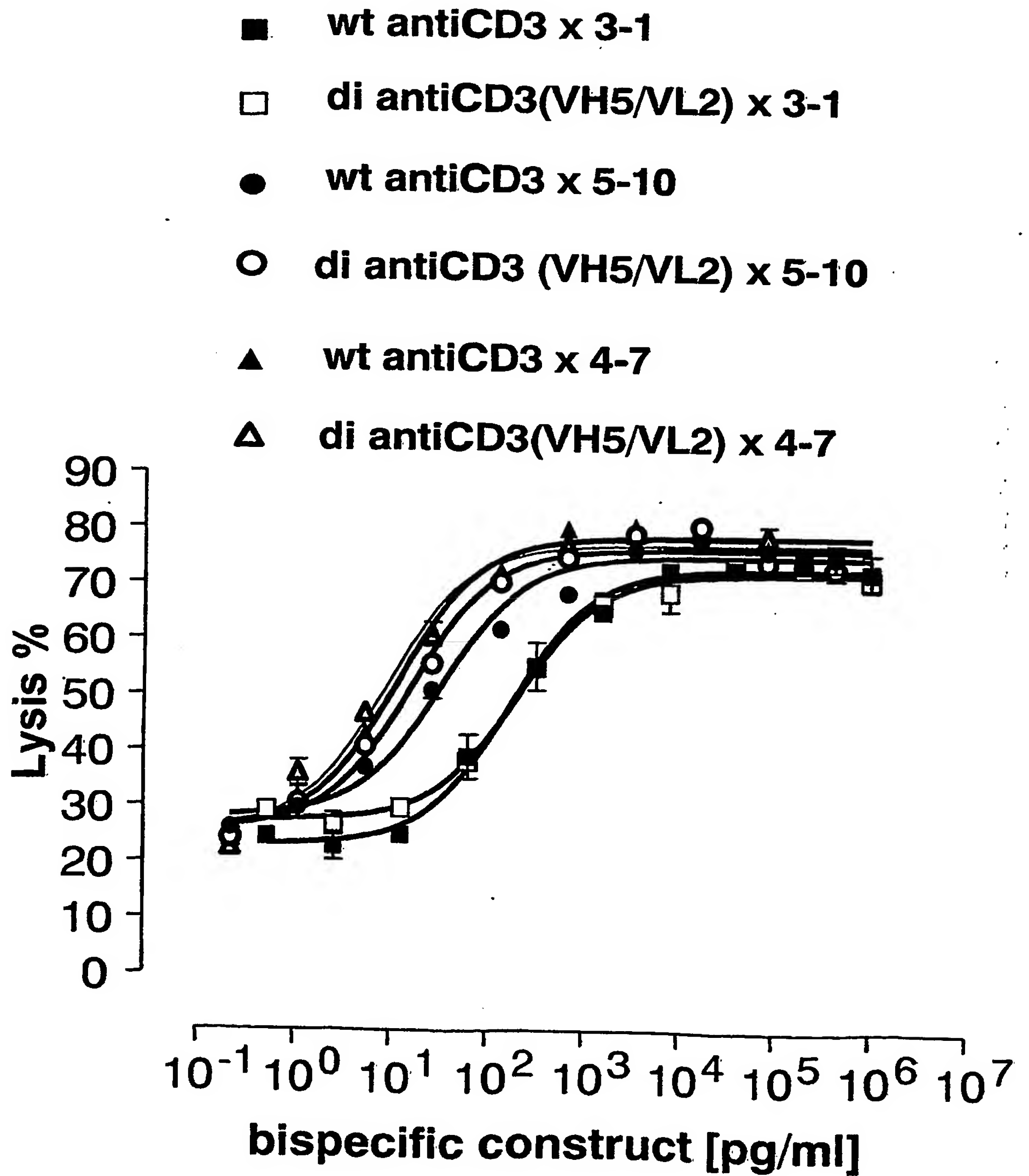
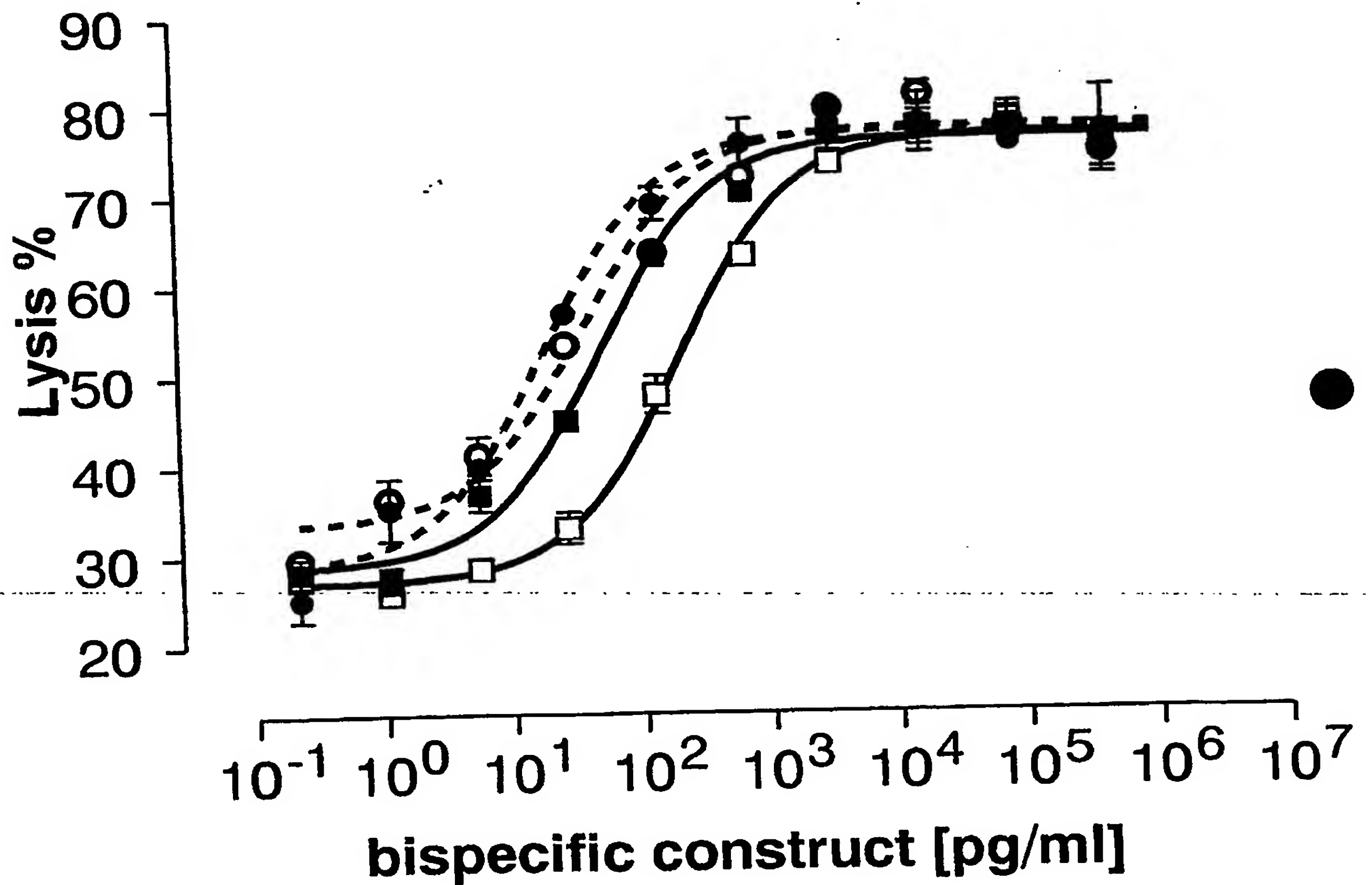
Figure 17

Figure 18

- 3-1 x antiCD3
- 3-1 x antiCD3(VH5/VL2)
- 5-10 x antiCD3
- 5-10 x antiCD3(VH5/VL2)



1
SEQUENCE LISTING

EPO - Munich
41
16. Okt. 2003

<110> Micromet AG

<120> Multispecific deimmunized CD3 binders

<130> G 2728 EP

<160> 409

<170> PatentIn version 3.1

<210> 1

<211> 729

<212> DNA

<213> artificial sequence

<220>

<223> wt Anti-CD3 cassette

<400> 1

gatatcaaac tgcagcagtc aggggctgaa ctggcaagac ctggggcctc agtgaagatg	60
tcctgcaaga cttctggcta cacctttact aggtacacga tgcactgggt aaaacagagg	120
cctggacagg gtctggaatg gattggatac attaatccta gccgtgggtta tactaattac	180
aatcagaagt tcaaggacaa ggccacattg actacagaca aatcctccag cacagcctac	240
atgcaactga gcagcctgac atctgaggac tctgcagtct attactgtgc aagatattat	300
gatgatcatt actgccttga ctactggggc caaggcacca ctctcacagt ctcctcagtc	360
gaaggtggaa gtggagggttc tgggtggaagt ggaggttcag gtggagtcga cgacattcag	420
ctgacccagt ctccagcaat catgtctgca tctccagggg agaaggtcac catgacctgc	480
agagccagtt caagtgtaag ttacatgaac tgggtaccagc agaagtcagg cacctcccc	540
aaaagatgga tttatgacac atccaaagtg gcttctggag tcccttatcg cttcagtggc	600
agtgggtctg ggacctcata ctctctcaca atcagcagca tggaggctga agatgctgcc	660
acttattact gccaacagtg gagtagtaac ccgctcacgt tcggtgctgg gaccaagctg	720
gagctgaaa	729

<210> 2

<211> 243

<212> PRT

<213> artificial sequence

<220>

<223> wt Anti-CD3 cassette

<400> 2

Asp Ile Lys Leu Gln Gln Ser Gly Ala Glu Leu Ala Arg Pro Gly Ala
1 5 10 15

Ser Val Lys Met Ser Cys Lys Thr Ser Gly Tyr Thr Phe Thr Arg Tyr
20 25 30

Thr Met His Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe
50 55 60

Lys Asp Lys Ala Thr Leu Thr Thr Asp Lys Ser Ser Ser Thr Ala Tyr
65 70 75 80

Met Gln Leu Ser Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Thr Leu Thr Val Ser Ser Val Glu Gly Gly Ser Gly Gly Ser Gly
115 120 125

Gly Ser Gly Gly Ser Gly Gly Val Asp Asp Ile Gln Leu Thr Gln Ser
130 135 140

Pro Ala Ile Met Ser Ala Ser Pro Gly Glu Lys Val Thr Met Thr Cys
145 150 155 160

Arg Ala Ser Ser Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Ser
165 170 175

Gly Thr Ser Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser
180 185 190

Gly Val Pro Tyr Arg Phe Ser Gly Ser Gly Ser Gly Thr Ser Tyr Ser
195 200 205

Leu Thr Ile Ser Ser Met Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys
210 215 220

Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe³ Gly Ala Gly Thr Lys Leu
225 230 235 240

Glu Leu Lys

<210> 3

<211> 18

<212> PRT

<213> artificial sequence

<220>

<223> deimmunized linker

<400> 3

Gly Glu Gly Thr Ser Thr Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly
1 5 10 15

Ala Asp

<210> 4

<211> 729

<212> DNA

<213> artificial sequence

<220>

<223> VH2/VL1

<400> 4

gacgtccaac	tggtgcagtc	aggggctgaa	gtgaaaaaac	ctggggcctc	agtgaagggtg	60
tcctgcaagg	cttctggcta	caccgctact	aggtacacga	tgcactgggt	aaggcaggca	120
cctggacagg	gtctggaatg	gattggatac	attaatccta	gccgtgggtta	tactaattac	180
gcacagaagt	tgcagggccg	cgtcacaatg	actacagaca	cttccaccag	cacagcctac	240
atggaactga	gcagcctgcg	ttctgaggac	actgcaacct	attactgtgc	aagatattat	300
gatgatcatt	actgccttga	ctactggggc	caaggcacca	cggtcaccgt	ctcctcaggc	360
gaagg tacta	gtactggttc	tggtggaagt	ggaggttcag	gtggagcaga	cgacattcag	420
atgacccagt	ctccatctag	cctgtctgca	tctgtcgggg	accgtgtcac	catcacctgc	480
agagccagtc	aaagtgtaag	ttacatgaac	tggtaccagc	agaagccggg	caaggcaccc	540
aaaagatgga	tttatgacac	atccaaagtg	gcttctggag	tccctgctcg	cttcagtggc	600
agtgggtctg	ggaccgacta	ctctctcaca	atcaacagct	tggaggctga	agatgctgcc	660

acttattact gccaacagtg gagtagtaac ccgctcacgt tcggtggcgg gaccaaggtg 720
gagatcaaa 729

<210> 5
<211> 243
<212> PRT
<213> artificial sequence

<220>
<223> VH2/VL1
<400> 5

Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Ala Thr Arg Tyr
20 25 30

Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Gln Lys Leu
50 55 60

Gln Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys
85 90 95

Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly
115 120 125

Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Gln Met Thr Gln Ser
130 135 140

Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys
145 150 155 160

Arg Ala Ser Gln Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro
165 170 175

Gly Lys Ala pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser
180 185 190

Gly Val Pro Ala Arg Phe Ser Gly Ser Gly⁵ Ser Gly Thr Asp Tyr Ser
195 200 205

Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys
210 215 220

Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
225 230 235 240

Glu Ile Lys

<210> 6

<211> 729

<212> DNA

<213> artificial sequence

<220>

<223> VH2/VL2

<400> 6

gacgtccaac	tggtgcagtc	aggggctgaa	gtgaaaaaac	ctggggcctc	agtgaagggtg	60
tcctgcaagg	cttctggcta	caccgctact	aggtacacga	tgcactgggt	aaggcaggca	120
cctggacagg	gtctggaatg	gattggatac	attaatccta	gccgtgggta	tactaattac	180
gcacagaagt	tgcagggccg	cgtcacaatg	actacagaca	cttccaccag	cacagcctac	240
atggaactga	gcagcctgcg	ttctgaggac	actgcaacct	attactgtgc	aagatattat	300
gatgatcatt	actgccttga	ctactggggc	caaggcacca	cggtcaccgt	ctcctcaggc	360
gaagg tacta	gtactggttc	tggtggaagt	ggagggttcag	gtggagcaga	cgacattgta	420
ctgacccagt	ctccagcaac	tctgtctctg	tctccagggg	agcgtgccac	cctgagctgc	480
agagccagtc	aaagtgtaag	ttacatgaac	tggtaccagc	agaagccggg	caaggcaccc	540
aaaagatgga	tttatgacac	atccaaagtg	gcttctggag	tccctgctcg	cttcagtggc	600
agtgggtctg	ggaccgacta	ctctctcaca	atcaacagct	tggaggctga	agatgctgcc	660
acttattact	gccaacagtg	gagtagtaac	ccgctcacgt	tcggtggcgg	gaccaagggtg	720
gagatcaaa						729

<210> 7

<211> 243

<212> PRT

<213> artificial sequence

<220>

<223> VH2/VL2

<400> 7

Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
 1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Ala Thr Arg Tyr
 20 25 30

Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
 35 40 45

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Gln Lys Leu
 50 55 60

Gln Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr
 65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys
 85 90 95

Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
 100 105 110

Thr Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly
 115 120 125

Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Val Leu Thr Gln Ser
 130 135 140

Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys
 145 150 155 160

Arg Ala Ser Gln Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro
 165 170 175

Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser
 180 185 190

Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser
 195 200 205

Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys
 210 215 220

Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
 225 230 235 240

Glu Ile Lys

<210> 8
 <211> 729
 <212> DNA
 <213> artificial sequence

<220>

<223> VH2/VL3

<400> 8

gacgtccaac	tggtgcagtc	aggggctgaa	gtgaaaaaac	ctggggcctc	agtgaagggtg	60
tcctgcaagg	cttctggcta	caccgctact	aggtacacga	tgcactgggt	aaggcaggca	120
cctggacagg	gtctggaatg	gattggatac	attaatccta	gccgtgggtta	tactaattac	180
gcacagaagt	tgcagggccg	cgtcacaatg	actacagaca	cttccaccag	cacagcctac	240
atggaactga	gcagcctgcg	ttctgaggac	actgcaacct	attactgtgc	aagatattat	300
gatgatcatt	actgccttga	ctactggggc	caaggcacca	cggtcacctg	ctcctcaggc	360
gaaggtacta	gtactggttc	tggtggaagt	ggagggttcag	gtggagcaga	cgacattgta	420
ctgacccagt	ctccagcaac	tctgtctctg	tctccagggg	agcgtgccac	cctgacctgc	480
agagccagtt	caagtgtaag	ttacatgaac	tggtaccagc	agaagccggg	caaggcaccc	540
aaaagatgga	tttatgacac	atccaaagtg	gcttctggag	tccttgctcg	cttcagtggc	600
agtgggtctg	ggaccgacta	ctctctcaca	atcaacagct	tggaggctga	agatgctgcc	660
acttattact	gccaacagtg	gagtagtaac	ccgctcacgt	tcggtggcgg	gaccaagggtg	720
gagatcaaa						729

<210> 9

<211> 243

<212> PRT

<213> artificial sequence

<220>

<223> VH2VL3

<400> 9

Asp	Val	Gln	Leu	Val	Gln	Ser	Gly	Ala	Glu	Val	Lys	Lys	Pro	Gly	Ala
1				5					10					15	
Ser	Val	Lys	Val	Ser	Cys	Lys	Ala	Ser	Gly	Tyr	Thr	Ala	Thr	Arg	Tyr
				20				25					30		
Thr	Met	His	Trp	Val	Arg	Gln	Ala	Pro	Gly	Gln	Gly	Leu	Glu	Trp	Ile
		35					40					45			

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Gln Lys Leu
 50 55 60

Gln Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr
 65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys
 85 90 95

Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
 100 105 110

Thr Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly
 115 120 125

Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Val Leu Thr Gln Ser
 130 135 140

Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Thr Cys
 145 150 155 160

Arg Ala Ser Ser Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro
 165 170 175

Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser
 180 185 190

Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser
 195 200 205

Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys
 210 215 220

Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
 225 230 235 240

Glu Ile Lys

<210> 10

<211> 729

<212> DNA

<213> artificial sequence

<220>

<223> VH3/VL1

<400> 10

gacgtccaac tgggtgcagtc aggggctgaa gtgaaaaaac ctggggcctc agtgaagggtg

tcctgcaagg cttctggcta caccgctact aggtacacga tgcactgggt aaggcaggca	120
cctggacagg gtctggaatg gattggatac attaatccta gccgtgggtta tactaattac	180
gcacagaagt tgcagggccg cgtcacaatg actacagaca cttccaccag cacagcctac	240
ctgcaaataa acagcctgaa aactgaggac actgcagtct attactgtgc aagatattat	300
gatgatcatt actgccttga ctactggggc caaggcacca cggtcaccgt ctcctcaggc	360
gaaggacta gtactgggtc tgggtggaagt ggagggttcag gtggagcaga cgacattcag	420
atgacccagt ctccatctag cctgtctgca tctgtcgggg accgtgtcac catcacctgc	480
agagccagtc aaagtgtaag ttacatgaac tgggtaccagc agaagccggg caaggcaccc	540
aaaagatgga tttatgacac atccaaagtg gcttctggag tccctgctcg cttcagtggc	600
agtgggtctg ggaccgacta ctctctcaca atcaacagct tggaggctga agatgctgcc	660
acttattact gccaacagtg gagtagtaac ccgctcacgt tcggtggcgg gaccaagggtg	720
gagatcaaa	729

<210> 11

<211> 243

<212> PRT

<213> artificial sequence

<220>

<223> VH3/VL1

<400> 11

Asp	Val	Gln	Leu	Val	Gln	Ser	Gly	Ala	Glu	Val	Lys	Lys	Pro	Gly	Ala
1			5						10					15	

Ser	Val	Lys	Val	Ser	Cys	Lys	Ala	Ser	Gly	Tyr	Thr	Ala	Thr	Arg	Tyr
			20					25					30		

Thr	Met	His	Trp	Val	Arg	Gln	Ala	Pro	Gly	Gln	Gly	Leu	Glu	Trp	Ile
		35					40					45			

Gly	Tyr	Ile	Asn	Pro	Ser	Arg	Gly	Tyr	Thr	Asn	Tyr	Ala	Gln	Lys	Leu
	50					55					60				

Gln	Gly	Arg	Val	Thr	Met	Thr	Thr	Asp	Thr	Ser	Thr	Ser	Thr	Ala	Tyr
65					70					75				80	

Leu	Gln	Met	Asn	Ser	Leu	Lys	Thr	Glu	Asp	Thr	Ala	Val	Tyr	Tyr	Cys
			85						90					95	

Ala	Arg	Tyr	Tyr	Asp	Asp	His	Tyr	Cys	Leu	Asp	Tyr	Trp	Gly	Gln	Gly
			100					105					110		

Thr Thr Val Thr Val Ser Ser Gly Glu Gly Thr ser Thr Gly Ser Gly
115 120 125

Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Gln Met Thr Gln Ser
130 135 140

Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys
145 150 155 160

Arg Ala Ser Gln Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro
165 170 175

Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser
180 185 190

Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser
195 200 205

Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys
210 215 220

Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
225 230 235 240

Glu Ile Lys

<210> 12

<211> 729

<212> DNA

<213> artificial sequence

<220>

<223> VH3/VL2

<400> 12

gacgtccaac tggtgcagtc aggggctgaa gtgaaaaaac ctggggcctc agtgaagggtg	60
tcctgcaagg cttctggcta caccgctact aggtacacga tgcactgggt aaggcaggca	120
cctggacagg gtctggaatg gattggatac attaatccta gccgtgggtta tactaattac	180
gcacagaagt tgcagggccg cgtcacaatg actacagaca cttccaccag cacagcctac	240
ctgcaaataga acagcctgaa aactgaggac actgcagtct attactgtgc aagatattat	300
gatgatcatt actgccttga ctactggggc caaggcacca cggtcaccgt ctcctcaggc	360
gaaggctacta gtactgggtc tggtggaagt ggaggttcag gtggagcaga cgacattgta	420
ctgacccagt ctccagcaac tctgtctctg tctccagggg agcgtgccac cctgagctgc	480
agagccagtc aaagtgtaag ttacatgaac tggtaccagc agaagccggg caaggcaccc	540

aaaagatgga tttatgacac atccaaagtg gcttctggag tccctgctcg cttcagtggc 600
 agtgggtctg ggaccgacta ctctctcaca atcaacagct tggaggctga agatgctgcc 660
 acttattact gccaacagtg gagtagtaac ccgctcacgt tcggtggcgg gaccaaggtg 720
 gagatcaaa 729

<210> 13

<211> 243

<212> PRT

<213> artificial sequence

<220>

<223> VH3/VL2

<400> 13

Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
 1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Ala Thr Arg Tyr
 20 25 30

Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
 35 40 45

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Gln Lys Leu
 50 55 60

Gln Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr
 65 70 75 80

Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr Tyr Cys
 85 90 95

Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
 100 105 110

Thr Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly
 115 120 125

Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Val Leu Thr Gln Ser
 130 135 140

Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys
 145 150 155 160

Arg Ala Ser Gln Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro
 165 170 175

Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser
 180 185 190

Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser
 195 200 205

Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys
 210 215 220

Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
 225 230 235 240

Glu Ile Lys

<210> 14

<211> 729

<212> DNA

<213> artificial sequence

<220>

<223> VH3/VL3

<400> 14
 gacgtccaac tgggtgcagtc aggggctgaa gtgaaaaaac ctggggcctc agtgaagggtg 60
 tcctgcaagg cttctggcta caccgctact aggtacacga tgcactgggt aaggcaggca 120
 cctggacagg gtctggaatg gattggatac attaatccta gccgtgggta tactaattac 180
 gcacagaagt tgcagggccg cgtcacaatg actacagaca cttccaccag cacagcctac 240
 ctgcaaatga acagcctgaa aactgaggac actgcagtct attactgtgc aagatattat 300
 gatgatcatt actgccttga ctactggggc caaggcacca cggtcaccgt ctcttcaggc 360
 gaaggtaact gtactgggttc tgggtggaagt ggagggttcag gtggagcaga cgacattgta 420
 ctgacccagt ctccagcaac tctgtctctg tctccagggg agcgtgccac cctgacctgc 480
 agagccagtt caagtgtaag ttacatgaac tgggtaccagc agaagccggg caaggcaccc 540
 aaaagatgga tttatgacac atccaaagtg gcttctggag tccctgctcg cttcagtggc 600
 agtgggtctg ggaccgacta ctctctcaca atcaacagct tggaggctga agatgctgcc 660
 acttattact gccaacagtg gagtagtaac ccgctcacgt tcggtggcgg gaccaagggtg 720
 gagatcaaa 729

<210> 15

<211> 243

<212> PRT

<213> artificial sequence

<220>

<223> VH3/VL3

<400> 15

Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Ala Thr Arg Tyr
20 25 30

Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Gln Lys Leu
50 55 60

Gln Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly
115 120 125

Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Val Leu Thr Gln Ser
130 135 140

Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Thr Cys
145 150 155 160

Arg Ala Ser Ser Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro
165 170 175

Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser
180 185 190

Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser
195 200 205

Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys
210 215 220

Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
225 230 235 240

Glu Ile Lys

<210> 16
 <211> 729
 <212> DNA
 <213> artificial sequence

<220>

<223> VH5/VL1

<400> 16
 gacgtccaac tgggtgcagtc aggggctgaa gtgaaaaaac ctggggcctc agtgaagggtg 60
 tcctgcaagg cttctggcta cacctttact aggtacacga tgcactgggt aaggcaggca 120
 cctggacagg gtctggaatg gattggatac attaatccta gccgtgggtta tactaattac 180
 gcagacagcg tcaagggccg cttcacaatc actacagaca aatccaccag cacagcctac 240
 atggaactga gcagcctgcg ttctgaggac actgcaacct attactgtgc aagatattat 300
 gatgatcatt actgccttga ctactggggc caaggcacca cggtcaccgt ctctcaggc 360
 gaagggtacta gtactggttc tgggtggaagt ggagggttcag gtggagcaga cgacattcag 420
 atgacccagt ctccatctag cctgtctgca tctgtcgggg accgtgtcac catcacctgc 480
 agagccagtc aaagtgtaag ttacatgaac tgggtaccagc agaagccggg caaggcaccc 540
 aaaagatgga tttatgacac atccaaagtg gcttctggag tccctgctcg cttcagtggc 600
 agtgggtctg ggaccgacta ctctctcaca atcaacagct tggaggctga agatgctgcc 660
 acttattact gccaacagtg gagtagtaac ccgctcacgt tcggtggcgg gaccaagggtg 720
 gagatcaaa 729

<210> 17
 <211> 243
 <212> PRT

~~<213> artificial sequence~~

<220>

<223> VH5/VL1

<400> 17

Asp val Gln Leu val Gln Ser Gly Ala Glu val Lys Lys Pro Gly Ala
 1 5 10 15

Ser val Lys val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr
 20 25 30

Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
 35 40 45

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val
 50 55 60

Lys Gly Arg Phe Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr
 65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys
 85 90 95

Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
 100 105 110

Thr Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly
 115 120 125

Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Gln Met Thr Gln Ser
 130 135 140

Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys
 145 150 155 160

Arg Ala Ser Gln Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro
 165 170 175

Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser
 180 185 190

Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser
 195 200 205

Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys
 210 215 220

Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
 225 230 235 240

Glu Ile Lys

<210> 18

<211> 729

<212> DNA

<213> artificial sequence

<220>

<223> VH5/VL2

<400> 18
 gacgtccaac tgggtgcagtc aggggctgaa gtgaaaaaac ctggggcctc agtgaagggtg 60
 tcctgcaagg cttctggcta cacctttact aggtacacga tgcactgggt aaggcaggca 120
 cctggacagg gtctggaatg gattggatac attaatccta gccgtgggtta tactaattac 180
 gcagacagcg tcaagggccg cttcacaatc actacagaca aatccaccag cacagcctac 240
 atggaactga gcagcctgcg ttctgaggac actgcaacct attactgtgc aagatattat 300
 gatgatcatt actgccttga ctactggggc caaggcacca cggtcaccgt ctcctcaggc 360
 gaagggtacta gtactgggtc tgggtggaagt ggagggttcag gtggagcaga cgacattgta 420
 ctgacccagt ctccagcaac tctgtctctg tctccagggg agcgtgccac cctgagctgc 480
 agagccagtc aaagtgtaag ttacatgaac tgggtaccagc agaagccggg caaggcaccc 540
 aaaagatgga tttatgacac atccaaagtg gcttctggag tccctgctcg cttcagtggc 600
 agtgggtctg ggaccgacta ctctctcaca atcaacagct tggaggctga agatgctgcc 660
 acttattact gccaacagtg gagtagtaac ccgctcacgt tcggtggcgg gaccaagggtg 720
 gagatcaaa 729

<210> 19

<211> 243

<212> PRT

<213> artificial sequence

<220>

<223> VH5/VL2

<400> 19

Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
 1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr
 20 25 30

Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
 35 40 45

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val
 50 55 60

Lys Gly Arg Phe Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr
 65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys
 85 90 95

Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
 100 105 110

Thr Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly
 115 120 125

Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Val Leu Thr Gln Ser
 130 135 140

Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys
 145 150 155 160

Arg Ala Ser Gln Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro
 165 170 175

Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser
 180 185 190

Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser
 195 200 205

Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys
 210 215 220

Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
 225 230 235 240

Glu Ile Lys

<210> 20

<211> 729

<212> DNA

<213> artificial sequence

<220>

<223> VH5/VL3

<400> 20

gacgtccaac tgggtgcagtc aggggctgaa gtgaaaaaac ctggggcctc agtgaagggtg	60
tcctgcaagg cttctggcta cacctttact aggtacacga tgcactgggt aaggcaggca	120
cctggacagg gtctggaatg gattggatac attaatccta gccgtgggta tactaattac	180
gcagacagcg tcaagggccg cttcacaatc actacagaca aatccaccag cacagcctac	240
atggaactga gcagcctgcg ttctgaggac actgcaacct attactgtgc aagatattat	300
gatgatcatt actgccttga ctactggggc caaggcacca cggtcaccgt ctctcaggc	360

18

gaaggtacta gtactgggttc tgggtggaagt ggaggttcag gtggagcaga cgacattgta	420
ctgacccagt ctccagcaac tctgtctctg tctccagggg agcgtgccac cctgacctgc	480
agagccagtt caagtgtaag ttacatgaac tgggtaccagc agaagccggg caaggcaccc	540
aaaagatgga tttatgacac atccaaagtg gcttctggag tccctgctcg cttcagtggc	600
agtgggtctg ggaccgacta ctctctcaca atcaacagct tggaggctga agatgctgcc	660
acttattact gccaacagtg gagtagtaac ccgctcacgt tcggtggcgg gaccaaggtg	720
gagatcaaa	729

<210> 21
 <211> 243
 <212> PRT
 <213> artificial sequence

<220>

<223> VH5/VL3

<400> 21

Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
 1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr
 20 25 30

Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
 35 40 45

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val
 50 55 60

Lys Gly Arg Phe Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr
 65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys
 85 90 95

Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
 100 105 110

Thr Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly
 115 120 125

Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Val Leu Thr Gln Ser
 130 135 140

Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Thr Cys
 145 150 155 160

Arg Ala Ser Ser Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro
 165 170 175

Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser
 180 185 190

Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser
 195 200 205

Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys
 210 215 220

Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
 225 230 235 240

Glu Ile Lys

<210> 22

<211> 729

<212> DNA

<213> artificial sequence

<220>

<223> VH7/VL1

<400> 22

gacgtccaac	tggtgcagtc	aggggctgaa	gtgaaaaaac	ctggggcctc	agtgaagggtg	60
tcctgcaagg	cttctggcta	cacctttact	aggtacacga	tgcactgggt	aaggcaggca	120
cctggacagg	gtctggaatg	gattggatac	attaatccta	gccgtgggta	tactaattac	180
aatcagaagt	tcaaggaccg	cgtcacaatc	actacagaca	aatccaccag	cacagcctac	240
atggaactga	gcagcctgcg	ttctgaggac	actgcagtct	attactgtgc	aagatattat	300
gatgatcatt	actgccttga	ctactggggc	caaggcacca	cggtcaccgt	ctcctcaggc	360
gaaggtacta	gtactggttc	tggtggaagt	ggagggttcag	gtggagcaga	cgacattcag	420
atgacccagt	ctccatctag	cctgtctgca	tctgtcgggg	accgtgtcac	catcacctgc	480
agagccagtc	aaagtgtaag	ttacatgaac	tggtaccagc	agaagccggg	caaggcacc	540
aaaagatgga	tttatgacac	atccaaagtg	gcttctggag	tccctgctcg	cttcagtggc	600
agtgggtctg	ggaccgacta	ctctctcaca	atcaacagct	tggaggctga	agatgctgcc	660
acttattact	gccaacagtg	gagtagtaac	ccgctcacgt	tcggtggcgg	gaccaagggtg	720
gagatcaaa						729

<210> 23

<211> 243

<212> PRT

<213> artificial sequence

<220>

<223> VH7/VL1

<400> 23

Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
 1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr
 20 25 30

Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
 35 40 45

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe
 50 55 60

Lys Asp Arg Val Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr
 65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
 85 90 95

Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
 100 105 110

Thr Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly
 115 120 125

Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Gln Met Thr Gln Ser
 130 135 140

Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys
 145 150 155 160

Arg Ala Ser Gln Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro
 165 170 175

Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser
 180 185 190

Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser
 195 200 205

Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys
 210 215 220

Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
 225 230 235 240

Glu Ile Lys

<210> 24

<211> 729

<212> DNA

<213> artificial sequence

<220>

<223> VH7/VL2

<400> 24

gacgtccaac	tggtgcagtc	aggggctgaa	gtgaaaaaac	ctggggcctc	agtgaagggtg	60
tcctgcaagg	cttctggcta	cacctttact	aggtacacga	tgcactgggt	aaggcaggca	120
cctggacagg	gtctggaatg	gattggatac	attaatccta	gccgtgggtta	tactaattac	180
aatcagaagt	tcaaggaccg	cgtcacaatc	actacagaca	aatccaccag	cacagcctac	240
atggaactga	gcagcctgcg	ttctgaggac	actgcagtct	attactgtgc	aagatattat	300
gatgatcatt	actgccttga	ctactggggc	caaggcacca	cggtcaccgt	ctcctcaggc	360
gaagggtacta	gtactggttc	tggtggaagt	ggagggttcag	gtggagcaga	cgacattgta	420
ctgacccagt	ctccagcaac	tctgtctctg	tctccagggg	agcgtgccac	cctgagctgc	480
agagccagtc	aaagtgtaag	ttacatgaac	tggtaccagc	agaagccggg	caaggcaccc	540
aaaagatgga	tttatgacac	atccaaagtg	gcttctggag	tccctgctcg	cttcagtggc	600
agtgggtctg	ggaccgacta	ctctctcaca	atcaacagct	tggaggctga	agatgctgcc	660
acttattact	gccaacagtg	gagtagtaac	ccgctcacgt	tcggtggcgg	gaccaagggtg	720
gagatcaaa						729

<210> 25

<211> 243

<212> PRT

<213> artificial sequence

<220>

<223> VH7/VL2

<400> 25

Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala

1 5 10 15 22
 Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr
 20 25 30
 Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
 35 40 45
 Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe
 50 55 60
 Lys Asp Arg Val Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr
 65 70 75 80
 Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
 85 90 95
 Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
 100 105 110
 Thr Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly
 115 120 125
 Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Val Leu Thr Gln Ser
 130 135 140
 Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys
 145 150 155 160
 Arg Ala Ser Gln Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro
 165 170 175
 Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser
 180 185 190
 Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser
 195 200 205
 Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys
 210 215 220
 Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
 225 230 235 240
 Glu Ile Lys

<210> 26

<211> 729

<212> DNA

<213> artificial sequence

<220>

<223> VH7/VL3

<400> 26

gacgtccaac	tggtgcagtc	aggggctgaa	gtgaaaaaac	ctggggcctc	agtgaagggtg	60
tcctgcaagg	cttctggcta	cacctttact	aggtacacga	tgcactgggt	aaggcaggca	120
cctggacagg	gtctggaatg	gattggatac	attaatccta	gccgtgggta	tactaattac	180
aatcagaagt	tcaaggaccg	cgtcacaatc	actacagaca	aatccaccag	cacagcctac	240
atggaactga	gcagcctgcg	ttctgaggac	actgcagtct	attactgtgc	aagatattat	300
gatgatcatt	actgccttga	ctactggggc	caaggcacca	cggtcaccgt	ctcctcaggc	360
gaaggtacta	gtactgggtc	tggtggaagt	ggagggttcag	gtggagcaga	cgacattgta	420
ctgacccagt	ctccagcaac	tctgtctctg	tctccagggg	agcgtgccac	cctgacctgc	480
agagccagtt	caagtgtaag	ttacatgaac	tggtaccagc	agaagccggg	caaggcaccc	540
aaaagatgga	tttatgacac	atccaaagtg	gcttctggag	tccctgctcg	cttcagtggc	600
agtgggtctg	ggaccgacta	ctctctcaca	atcaacagct	tggaggctga	agatgctgcc	660
acttattact	gccaacagtg	gagtagtaac	ccgctcacgt	tcggtggcgg	gaccaagggtg	720
gagatcaaa						729

<210> 27

<211> 243

<212> PRT

<213> artificial sequence

<220>

<223> VH7/VL3

<400> 27

Asp	Val	Gln	Leu	Val	Gln	Ser	Gly	Ala	Glu	Val	Lys	Lys	Pro	Gly	Ala	1	5	10	15
Ser	Val	Lys	Val	Ser	Cys	Lys	Ala	Ser	Gly	Tyr	Thr	Phe	Thr	Arg	Tyr	20	25	30	
Thr	Met	His	Trp	Val	Arg	Gln	Ala	Pro	Gly	Gln	Gly	Leu	Glu	Trp	Ile	35	40	45	
Gly	Tyr	Ile	Asn	Pro	Ser	Arg	Gly	Tyr	Thr	Asn	Tyr	Asn	Gln	Lys	Phe	50	55	60	
Lys	Asp	Arg	Val	Thr	Ile	Thr	Thr	Asp	Lys	Ser	Thr	Ser	Thr	Ala	Tyr				

65		70		24 75		80									
Met	Glu	Leu	Ser	Ser	Leu	Arg	Ser	Glu	Asp	Thr	Ala	Val	Tyr	Tyr	Cys
			85						90					95	
Ala	Arg	Tyr	Tyr	Asp	Asp	His	Tyr	Cys	Leu	Asp	Tyr	Trp	Gly	Gln	Gly
			100					105					110		
Thr	Thr	Val	Thr	Val	Ser	Ser	Gly	Glu	Gly	Thr	Ser	Thr	Gly	Ser	Gly
		115					120					125			
Gly	Ser	Gly	Gly	Ser	Gly	Gly	Ala	Asp	Asp	Ile	Val	Leu	Thr	Gln	Ser
	130					135					140				
Pro	Ala	Thr	Leu	Ser	Leu	Ser	Pro	Gly	Glu	Arg	Ala	Thr	Leu	Thr	Cys
	145				150					155					160
Arg	Ala	Ser	Ser	Ser	Val	Ser	Tyr	Met	Asn	Trp	Tyr	Gln	Gln	Lys	Pro
				165					170					175	
Gly	Lys	Ala	Pro	Lys	Arg	Trp	Ile	Tyr	Asp	Thr	Ser	Lys	Val	Ala	Ser
			180					185					190		
Gly	Val	Pro	Ala	Arg	Phe	Ser	Gly	Ser	Gly	Ser	Gly	Thr	Asp	Tyr	Ser
		195					200					205			
Leu	Thr	Ile	Asn	Ser	Leu	Glu	Ala	Glu	Asp	Ala	Ala	Thr	Tyr	Tyr	Cys
	210					215				220					
Gln	Gln	Trp	Ser	Ser	Asn	Pro	Leu	Thr	Phe	Gly	Gly	Gly	Thr	Lys	Val
	225				230					235					240

Glu Ile Lys

<210> 28

<211> 20

<212> DNA

<213> artificial sequence

<220>

<223> Sequencing primer

<400> 28
cctcagacag tggttcaaag

<210> 29

<211> 18

<212> DNA

<213> artificial sequence

<220>

<223> Sequencing primer

<400> 29

agccgccacg tgggcctc

18

<210> 30

<211> 1473

<212> DNA

<213> artificial sequence

<220>

<223> anti-CD3 VH5/VL2 x 3-1 VHVL

<400> 30

gacgtccaac tgggtgcagtc aggggctgaa gtgaaaaaac ctggggcctc agtgaagggtg	60
tcctgcaagg cttctggcta cacctttact aggtacacga tgcactgggt aaggcaggca	120
cctggacagg gtctggaatg gattggatac attaatccta gccgtgggtta tactaattac	180
gcagacagcg tcaagggccg cttcacaatc actacagaca aatccaccag cacagcctac	240
atggaactga gcagcctgcg ttctgaggac actgcaacct attactgtgc aagatattat	300
gatgatcatt actgccttga ctactggggc caaggcacca cggtcaccgt ctcctcaggc	360
gaagggtacta gtactggttc tgggtggaagt ggaggttcag gtggagcaga cgacattgta	420
ctgacccagt ctccagcaac tctgtctctg tctccagggg agcgtgccac cctgagctgc	480
agagccagtc aaagtgtaag ttacatgaac tgggtaccagc agaagccggg caaggcaccc	540
aaaagatgga tttatgacac atccaaagtg gcttctggag tccctgctcg cttcagtggc	600
agtgggtctg ggaccgacta ctctctcaca atcaacagct tggaggctga agatgctgcc	660
acttattact gccaacagtg gagtagtaac ccgctcacgt tcggtggcgg gaccaagggtg	720
gagatcaaat ccggagggtg tggatccgag gtgcagctgc tcgagcagtc tggagctgag	780
ctggtgaaac ctggggcctc agtgaagata tcctgcaagg cttctggata cgccttcact	840
aactactggc taggttgggt aaagcagagg cctggacatg gacttgagtg gattggagat	900
cttttcctg gaagtggtaa tactcactac aatgagagggt tcaggggcaa agccacactg	960
actgcagaca aatcctcgag cacagccttt atgcagctca gtagcctgac atctgaggac	1020
tctgctgtct atttctgtgc aagattgagg aactgggacg aggctatgga ctactggggc	1080
caagggacca cggtcaccgt ctcctcagggt ggtgggtggt ctggcggcgg cggtccggt	1140
ggtgggtggt ctgagctcgt catgacccag tctccatctt atcttgctgc atctcctgga	1200

26

gaaaccatta ctattaattg cagggcaagt aagagcatta gcaaataattt agcctgggtat	1260
caagagaaac ctgggaaaac taataagctt cttatctact ctggatccac tttgcaatct	1320
ggaattccat caaggttcag tggcagtgga tctgggtacag atttcactct caccatcagt	1380
agcctggagc ctgaagattt tgcaatgtat tactgtcaac agcataatga atatccgtac	1440
acgttcggag gggggaccaa gcttgagatc aaa	1473

<210> 31
 <211> 491
 <212> PRT
 <213> artificial sequence

<220>

<223> anti-CD3 VH5/VL2 x 3-1 VHVL

<400> 31

Asp val Gln Leu val Gln Ser Gly Ala Glu val Lys Lys Pro Gly Ala
 1 5 10 15

Ser val Lys val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr
 20 25 30

Thr Met His Trp val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
 35 40 45

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser val
 50 55 60

Lys Gly Arg Phe Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr
 65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys
 85 90 95

Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
 100 105 110

Thr Thr val Thr val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly
 115 120 125

Gly ser Gly Gly Ser Gly Gly Ala Asp Asp Ile val Leu Thr Gln Ser
 130 135 140

Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys
 145 150 155 160

Arg Ala Ser Gln Ser val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro
 165 170 175

Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser
 180 185 190
 Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser
 195 200 205
 Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys
 210 215 220
 Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
 225 230 235 240
 Glu Ile Lys Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Leu Glu Gln
 245 250 255
 Ser Gly Ala Glu Leu Val Lys Pro Gly Ala Ser Val Lys Ile Ser Cys
 260 265 270
 Lys Ala Ser Gly Tyr Ala Phe Thr Asn Tyr Trp Leu Gly Trp Val Lys
 275 280 285
 Gln Arg Pro Gly His Gly Leu Glu Trp Ile Gly Asp Leu Phe Pro Gly
 290 295 300
 Ser Gly Asn Thr His Tyr Asn Glu Arg Phe Arg Gly Lys Ala Thr Leu
 305 310 315 320
 Thr Ala Asp Lys Ser Ser Ser Thr Ala Phe Met Gln Leu Ser Ser Leu
 325 330 335
 Thr Ser Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg Leu Arg Asn Trp
 340 345 350
 Asp Glu Ala Met Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser
 355 360 365
 Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
 370 375 380
 Glu Leu Val Met Thr Gln Ser Pro Ser Tyr Leu Ala Ala Ser Pro Gly
 385 390 395 400
 Glu Thr Ile Thr Ile Asn Cys Arg Ala Ser Lys Ser Ile Ser Lys Tyr
 405 410 415
 Leu Ala Trp Tyr Gln Glu Lys Pro Gly Lys Thr Asn Lys Leu Leu Ile
 420 425 430
 Tyr Ser Gly Ser Thr Leu Gln Ser Gly Ile Pro Ser Arg Phe Ser Gly
 435 440 445

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Glu Pro
 450 455 460

Glu Asp Phe Ala Met Tyr Tyr Cys Gln Gln His Asn Glu Tyr Pro Tyr
 465 470 475 480

Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
 485 490

<210> 32

<211> 1500

<212> DNA

<213> artificial sequence

<220>

<223> anti-CD3 VH5/VL2 x 4-7 VHVL

<400> 32
 gacgtccaac tgggtgcagtc aggggctgaa gtgaaaaaac ctggggcctc agtgaagggtg 60
 tcctgcaagg cttctggcta cacctttact aggtacacga tgcactgggt aaggcaggca 120
 cctggacagg gtctggaatg gattggatac attaattccta gccgtgggtta tactaattac 180
 gcagacagcg tcaagggccg cttcacaatc actacagaca aatccaccag cacagcctac 240
 atggaactga gcagcctgcg ttctgaggac actgcaacct attactgtgc aagatattat 300
 gatgatcatt actgccttga ctactggggc caaggcacca cggtcaccgt ctccctcaggc 360
 gaagggtacta gtactgggtc tgggtggaagt ggagggttcag gtggagcaga cgacattgta 420
 ctgacccagt ctccagcaac tctgtctctg tctccagggg agcgtgccac cctgagctgc 480
 agagccagtc aaagtgtaag ttacatgaac tgggtaccagc agaagccggg caaggcaccc 540
 aaaagatgga tttatgacac atccaaagtg gcttctggag tccctgctcg cttcagtggc 600
 agtgggtctg ggaccgacta ctctctcaca atcaacagct tggaggctga agatgctgcc 660
 acttattact gccaacagtg gagtagtaac ccgctcacgt tcggtggcgg gaccaagggtg 720
 gagatcaaat ccggagggtg tggatccgag gtgcagctgc tcgagcagtc tggagctgag 780
 ctggcgaggc ctggggcttc agtgaagctg tcctgcaagg cttctggcta caccttcaca 840
 aactatgggt taagctgggt gaagcagagg cctggacagg tccttgagtg gattggagag 900
 gtttatccta gaattggtaa tgcttactac aatgagaagt tcaagggcaa ggccacactg 960
 actgcagaca aatcctccag cacagcgtcc atggagctcc gcagcctgac ctctgaggac 1020
 tctgcgggtct atttctgtgc aagacgggga tcctacgata ctaactacga ctgggtacttc 1080
 gatgtctggg gccaaaggac cacggtcacc gtctcctcag gtgggtgggtg ttctggcggc 1140
 ggcggtccg gtgggtgggtg ttctgagctc gtgatgacct agactccact ctccctgcct 1200
 gtcagtcttg gagatcaagc ctccatctct tgcagatcta gtcagagcct tgtacacagt 1260

aatggaaaca cctattttaca ttggtacctg cagaagccag gccagtcctcc aaagctcctg 1320
 atctacaaag tttccaaccg attttctggg gtcccagaca ggttcagtgg cagtggatca 1380
 gggacagatt tcacactcaa gatcagcaga gtggaggctg aggatctggg agttttatttc 1440
 tgctctcaaa gtacacatgt tccgtacacg ttcggagggg ggaccaagct tgagatcaaa 1500

<210> 33

<211> 500

<212> PRT

<213> artificial sequence

<220>

<223> anti-CD3 VH5/VL2 x 4-7 VHVL

<400> 33

Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
 1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr
 20 25 30

Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
 35 40 45

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val
 50 55 60

Lys Gly Arg Phe Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr
 65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys
 85 90 95

Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
 100 105 110

Thr Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly
 115 120 125

Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Val Leu Thr Gln Ser
 130 135 140

Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys
 145 150 155 160

Arg Ala Ser Gln Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro
 165 170 175

Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser
 180 185 190

Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser
 195 200 205

Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys
 210 215 220

Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
 225 230 235 240

Glu Ile Lys Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Leu Glu Gln
 245 250 255

Ser Gly Ala Glu Leu Ala Arg Pro Gly Ala Ser Val Lys Leu Ser Cys
 260 265 270

Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr Gly Leu Ser Trp Val Lys
 275 280 285

Gln Arg Pro Gly Gln Val Leu Glu Trp Ile Gly Glu Val Tyr Pro Arg
 290 295 300

Ile Gly Asn Ala Tyr Tyr Asn Glu Lys Phe Lys Gly Lys Ala Thr Leu
 305 310 315 320

Thr Ala Asp Lys Ser Ser Ser Thr Ala Ser Met Glu Leu Arg Ser Leu
 325 330 335

Thr Ser Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg Arg Gly Ser Tyr
 340 345 350

Asp Thr Asn Tyr Asp Trp Tyr Phe Asp Val Trp Gly Gln Gly Thr Thr
 355 360 365

Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Ser Gly
 370 375 380

Gly Gly Gly Ser Glu Leu Val Met Thr Gln Thr Pro Leu Ser Leu Pro
 385 390 395 400

Val Ser Leu Gly Asp Gln Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser
 405 410 415

Leu Val His Ser Asn Gly Asn Thr Tyr Leu His Trp Tyr Leu Gln Lys
 420 425 430

Pro Gly Gln Ser Pro Lys Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe
 435 440 445

Ser Gly Val Pro Asp Arg Phe Ser Gly Ser³¹ Gly Ser Gly Thr Asp Phe
450 455 460

Thr Leu Lys Ile Ser Arg Val Glu Ala Glu Asp Leu Gly Val Tyr Phe
465 470 475 480

Cys Ser Gln Ser Thr His Val Pro Tyr Thr Phe Gly Gly Gly Thr Lys
485 490 495

Leu Glu Ile Lys
500

<210> 34

<211> 1500

<212> DNA

<213> artificial sequence

<220>

<223> anti-CD3 VH5/VL2 x 4-7 VLVH

<400> 34

gacgtccaac	tggtgcagtc	aggggctgaa	gtgaaaaaac	ctggggcctc	agtgaagggtg	60
tcctgcaagg	cttctggcta	cacctttact	aggtacacga	tgcactgggt	aaggcaggca	120
cctggacagg	gtctggaatg	gattggatac	attaatccta	gccgtgggtta	tactaattac	180
gcagacagcg	tcaagggccg	cttcacaatc	actacagaca	aatccaccag	cacagcctac	240
atggaactga	gcagcctgcg	ttctgaggac	actgcaacct	attactgtgc	aagatattat	300
gatgatcatt	actgccttga	ctactggggc	caaggcacca	cggtcaccgt	ctcctcaggc	360
gaaggtacta	gtactgggtc	tggtggaagt	ggaggttcag	gtggagcaga	cgacattgta	420
ctgacccagt	ctccagcaac	tctgtctctg	tctccagggg	agcgtgccac	cctgagctgc	480
agagccagtc	aaagtgtgtaag	ttacatgaac	tggtaccagc	agaagccggg	caaggcaccc	540
aaaagatgga	tttatgacac	atccaaagtg	gcttctggag	tccctgctcg	cttcagtggc	600
agtgggtctg	ggaccgacta	ctctctcaca	atcaacagct	tggaggctga	agatgctgcc	660
acttattact	gccaacagtg	gagtagtaac	ccgctcacgt	tcggtggcgg	gaccaagggtg	720
gagatcaa	atccggagggtg	tggtatccgag	ctcgtgatga	cccagactcc	actctccctg	780
cctgtcagtc	ttggagatca	agcctccatc	tcttgcagat	ctagtcagag	ccttgtacac	840
agtaatggaa	acacctat	ttacattggtac	ctgcagaagc	caggccagtc	tccaaagctc	900
ctgatctaca	aagtttccaa	ccgattttct	gggggtcccag	acagggttcag	tggcagtggg	960
tcagggacag	atttcacact	caagatcagc	agagtggagg	ctgaggatct	gggagtttat	1020
ttctgctctc	aaagtacaca	tgttccgtac	acgttcggag	gggggaccaa	gcttgagatc	1080
aaagggtggtg	gtggttctg	cggcggcggc	tccggtggtg	gtggttctga	ggtgcagctg	1140

ctcgagcagt ctggagctga gctggcgagg cctgggggctt cagtgaagct gtcctgcaag 1200
 gcttctgggt acaccttcac aaactatggt ttaagctggg tgaagcagag gcctggacag 1260
 gtccttgagt ggattggaga ggtttatcct agaattggta atgcttacta caatgagaag 1320
 ttcaagggca aggccacact gactgcagac aaatcctcca gcacagcgtc catggagctc 1380
 cgcagcctga cctctgagga ctctgcggtc tatttctgtg caagacgggg atcctacgat 1440
 actaactacg actggtactt cgatgtctgg ggccaaggga ccacgggtcac cgtctcctca 1500

<210> 35

<211> 500

<212> PRT

<213> artificial sequence

<220>

<223> anti-CD3 VH5/VL2 x 4-7 VLVH

<400> 35

Asp val Gln Leu val Gln Ser Gly Ala Glu val Lys Lys Pro Gly Ala
 1 5 10 15

Ser val Lys val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr
 20 25 30

Thr Met His Trp val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
 35 40 45

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser val
 50 55 60

Lys Gly Arg Phe Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr
 65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys
 85 90 95

Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
 100 105 110

Thr Thr val Thr val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly
 115 120 125

Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile val Leu Thr Gln Ser
 130 135 140

Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys
 145 150 155 160

Arg Ala Ser Gln Ser Val Ser Tyr Met Asn³³ Trp Tyr Gln Gln Lys Pro
 165 170 175
 Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser
 180 185 190
 Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Thr Asp Tyr Ser
 195 200 205
 Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys
 210 215 220
 Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
 225 230 235 240
 Glu Ile Lys Ser Gly Gly Gly Gly Ser Glu Leu Val Met Thr Gln Thr
 245 250 255
 Pro Leu Ser Leu Pro Val Ser Leu Gly Asp Gln Ala Ser Ile Ser Cys
 260 265 270
 Arg Ser Ser Gln Ser Leu Val His Ser Asn Gly Asn Thr Tyr Leu His
 275 280 285
 Trp Tyr Leu Gln Lys Pro Gly Gln Ser Pro Lys Leu Leu Ile Tyr Lys
 290 295 300
 Val Ser Asn Arg Phe Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly
 305 310 315 320
 Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu Asp
 325 330 335
 Leu Gly Val Tyr Phe Cys Ser Gln Ser Thr His Val Pro Tyr Thr Phe
 340 345 350
 Gly Gly Gly Thr Lys Leu Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly
 355 360 365
 Gly Gly Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Leu Glu Gln Ser
 370 375 380
 Gly Ala Glu Leu Ala Arg Pro Gly Ala Ser Val Lys Leu Ser Cys Lys
 385 390 395 400
 Ala Ser Gly Tyr Thr Phe Thr Asn Tyr Gly Leu Ser Trp Val Lys Gln
 405 410 415
 Arg Pro Gly Gln Val Leu Glu Trp Ile Gly Glu Val Tyr Pro Arg Ile
 420 425 430
 Gly Asn Ala Tyr Tyr Asn Glu Lys Phe Lys Gly Lys Ala Thr Leu Thr

435 440 445
 Ala Asp Lys Ser Ser Ser Thr Ala Ser Met Glu Leu Arg Ser Leu Thr
 450 455 460
 Ser Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg Arg Gly Ser Tyr Asp
 465 470 475 480
 Thr Asn Tyr Asp Trp Tyr Phe Asp Val Trp Gly Gln Gly Thr Thr Val
 485 490 495
 Thr Val Ser Ser
 500

<210> 36

<211> 1491

<212> DNA

<213> artificial sequence

<220>

<223> anti-CD3 VH5/VL2 x 5-10 VHVL

<400> 36
 gacgtccaac tgggtgcagtc aggggctgaa gtgaaaaaac ctggggcctc agtgaagggtg 60
 tcctgcaagg cttctggcta cacctttact aggtacacga tgcactgggt aaggcaggca 120
 cctggacagg gtctggaatg gattggatac attaatccta gccgtgggtta tactaattac 180
 gcagacagcg tcaagggccg cttcacaatc actacagaca aatccaccag cacagcctac 240
 atggaactga gcagcctgcg ttctgaggac actgcaacct attactgtgc aagatattat 300
 gatgatcatt actgccttga ctactggggc caaggcacca cggtcacctg ctctcaggc 360
 gaaggtaact gtactgggtc tgggtggaagt ggagggttcag gtggagcaga cgacattgta 420
 ctgacccagt ctccagcaac tctgtctctg tctccagggg agcgtgccac cctgagctgc 480
 agagccagtc aaagtgtaag ttacatgaac tgggtaccagc agaagccggg caaggcaccc 540
 aaaagatgga tttatgacac atccaaagtg gcttctggag tccctgctcg cttcagtggc 600
 agtgggtctg ggaccgacta ctctctcaca atcaacagct tggaggctga agatgctgcc 660
 acttattact gccaacagtg gagtagtaac ccgctcacgt tcggtggcgg gaccaagggtg 720
 gagatcaaatt ccggagggtg tggatccgag gtgcagctgc tcgagcagtc tggagctgag 780
 ctggtaaggc ctgggacttc agtgaagata tcctgcaagg cttctggata cgccttcact 840
 aactactggc taggttgggt aaagcagagg cctggacatg gacttgagt gattggagat 900
 attttccctg gaagtggtaa tatccactac aatgagaagt tcaagggcaa agccacactg 960
 actgcagaca aatcttcgag cacagcctat atgcagctca gtagcctgac atttgaggac 1020
 tctgctgtct atttctgtgc aagactgagg aactgggacg agcctatgga ctactggggc 1080

caagggacca cggtcaccgt ctcctcaggt ggtggtggtt ctggcggcgg cggctccggt 1140
 ggtggtggtt ctgagctcgt gatgacacag tctccatcct ccctgactgt gacagcagga 1200
 gagaagggtca ctatgagctg caagtccagt cagagtctgt taaacagtgg aaatcaaaag 1260
 aactacttga cctggtacca gcagaaacca gggcagcctc ctaaactggt gatctactgg 1320
 gcatccacta ggggaatctgg ggtccctgat cgcttcacag gcagtggatc tggaacagat 1380
 ttcacttctca ccatcagcag tgtgcaggct gaagacctgg cagtttatta ctgtcagaat 1440
 gattatagtt atccgctcac gttcgggtgct gggaccaagc ttgagatcaa a 1491

<210> 37

<211> 497

<212> PRT

<213> artificial sequence

<220>

<223> anti-CD3 VH5/VL2 x 5-10 VHVL

<400> 37

Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
 1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr
 20 25 30

Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
 35 40 45

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val
 50 55 60

Lys Gly Arg Phe Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr
 65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys
 85 90 95

Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
 100 105 110

Thr Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly
 115 120 125

Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Val Leu Thr Gln Ser
 130 135 140

Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys

145 150 36 155 160

Arg Ala Ser Gln Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro
165 170 175

Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser
180 185 190

Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser
195 200 205

Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys
210 215 220

Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
225 230 235 240

Glu Ile Lys Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Leu Glu Gln
245 250 255

Ser Gly Ala Glu Leu Val Arg Pro Gly Thr Ser Val Lys Ile Ser Cys
260 265 270

Lys Ala Ser Gly Tyr Ala Phe Thr Asn Tyr Trp Leu Gly Trp Val Lys
275 280 285

Gln Arg Pro Gly His Gly Leu Glu Trp Ile Gly Asp Ile Phe Pro Gly
290 295 300

Ser Gly Asn Ile His Tyr Asn Glu Lys Phe Lys Gly Lys Ala Thr Leu
305 310 315 320

Thr Ala Asp Lys Ser Ser Ser Thr Ala Tyr Met Gln Leu Ser Ser Leu
325 330 335

Thr Phe Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg Leu Arg Asn Trp
340 345 350

Asp Glu Pro Met Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser
355 360 365

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
370 375 380

Glu Leu Val Met Thr Gln Ser Pro Ser Ser Leu Thr Val Thr Ala Gly
385 390 395 400

Glu Lys Val Thr Met Ser Cys Lys Ser Ser Gln Ser Leu Leu Asn Ser
405 410 415

Gly Asn Gln Lys Asn Tyr Leu Thr Trp Tyr Gln Gln Lys Pro Gly Gln
420 425 430

Pro Pro Lys Leu Leu Ile Tyr Trp Ala Ser Thr Arg Glu Ser Gly Val
 435 440 445

Pro Asp Arg Phe Thr Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
 450 455 460

Ile Ser Ser Val Gln Ala Glu Asp Leu Ala Val Tyr Tyr Cys Gln Asn
 465 470 475 480

Asp Tyr Ser Tyr Pro Leu Thr Phe Gly Ala Gly Thr Lys Leu Glu Ile
 485 490 495

Lys

<210> 38

<211> 1491

<212> DNA

<213> artificial sequence

<220>

<223> anti-CD3 VH5/VL2 x 5-10 VLVH

<400> 38

gacgtccaac	tggtgcagtc	aggggctgaa	gtgaaaaaac	ctggggcctc	agtgaagggtg	60
tcctgcaagg	cttctggcta	cacctttact	aggtacacga	tgcactgggt	aaggcaggca	120
cctggacagg	gtctggaatg	gattggatac	attaatccta	gccgtgggta	tactaattac	180
gcagacagcg	tcaagggccg	cttcacaatc	actacagaca	aatccaccag	cacagcctac	240
atggaactga	gcagcctgcg	ttctgaggac	actgcaacct	attactgtgc	aagatattat	300
gatgatcatt	actgccttga	ctactggggc	caaggcacca	cggtcaccgt	ctcctcaggc	360
gaagg tacta	gtactgggtc	tggtggaagt	ggagggttcag	gtggagcaga	cgacattgta	420
ctgacccagt	ctccagcaac	tctgtctctg	tctccagggg	agcgtgccac	cctgagctgc	480
agagccagtc	aaagtgtaag	ttacatgaac	tggtaccagc	agaagccggg	caaggcaccc	540
aaaagatgga	tttatgacac	atccaaagtg	gcttctggag	tccctgctcg	cttcagtggc	600
agtgggtctg	ggaccgacta	ctctctcaca	atcaacagct	tggaggctga	agatgctgcc	660
acttattact	gccaacagtg	gagtagtaac	ccgctcacgt	tcggtggcgg	gaccaagggtg	720
gagatcaa at	ccggagggtg	tggatccgag	ctcgtgatga	cacagtctcc	atcctccctg	780
actgtgacag	caggagagaa	ggtcactatg	agctgcaagt	ccagtcagag	tctgttaaac	840
agtggaaatc	aaaagaacta	cttgacctgg	taccagcaga	aaccagggca	gcctcctaaa	900
ctgttgatct	actgggcatc	cactagggaa	tctgggggtcc	ctgatcgctt	cacaggcagt	960

38

ggatctggaa cagatttcac tctcaccatc agcagtgtgc aggctgaaga cctggcagtt	1020
tattactgtc agaatgatta tagttatccg ctcacgttcg gtgctgggac caagcttgag	1080
atcaaagggtg gtggtgggttc tggcggcggc ggctccgggtg gtggtgggttc tgagggtgcag	1140
ctgctcgagc agtctggagc tgagctggta aggcctggga cttcagtgaa gatatacctgc	1200
aaggcttctg gatacgcctt cactaactac tggctagggtt gggtaaagca gaggcctgga	1260
catggacttg agtggattgg agatattttc cctggaagtg gtaatatcca ctacaatgag	1320
aagttcaagg gcaaagccac actgactgca gacaaatctt cgagcacagc ctatatgcag	1380
ctcagtagcc tgacatttga ggactctgct gtctattttct gtgcaagact gaggaactgg	1440
gacgagccta tggactactg gggccaaggg accacgggtca ccgtctcctc a	1491

<210> 39

<211> 497

<212> PRT

<213> artificial sequence

<220>

<223> anti-CD3 VH5/VL2 x 5-10 VLVH

<400> 39

Asp	Val	Gln	Leu	Val	Gln	Ser	Gly	Ala	Glu	Val	Lys	Lys	Pro	Gly	Ala
1				5					10					15	

Ser	Val	Lys	Val	Ser	Cys	Lys	Ala	Ser	Gly	Tyr	Thr	Phe	Thr	Arg	Tyr
			20					25					30		

Thr	Met	His	Trp	Val	Arg	Gln	Ala	Pro	Gly	Gln	Gly	Leu	Glu	Trp	Ile
		35					40					45			

Gly	Tyr	Ile	Asn	Pro	Ser	Arg	Gly	Tyr	Thr	Asn	Tyr	Ala	Asp	Ser	Val
	50					55					60				

Lys	Gly	Arg	Phe	Thr	Ile	Thr	Thr	Asp	Lys	Ser	Thr	Ser	Thr	Ala	Tyr
65					70					75					80

Met	Glu	Leu	Ser	Ser	Leu	Arg	Ser	Glu	Asp	Thr	Ala	Thr	Tyr	Tyr	Cys
				85					90					95	

Ala	Arg	Tyr	Tyr	Asp	Asp	His	Tyr	Cys	Leu	Asp	Tyr	Trp	Gly	Gln	Gly
			100					105					110		

Thr	Thr	Val	Thr	Val	Ser	Ser	Gly	Glu	Gly	Thr	Ser	Thr	Gly	Ser	Gly
		115					120					125			

Gly	Ser	Gly	Gly	Ser	Gly	Gly	Ala	Asp	Asp	Ile	Val	Leu	Thr	Gln	Ser
	130					135					140				

Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys
 145 150 155 160
 Arg Ala Ser Gln Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro
 165 170 175
 Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser
 180 185 190
 Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser
 195 200 205
 Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys
 210 215 220
 Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
 225 230 235 240
 Glu Ile Lys Ser Gly Gly Gly Gly Ser Glu Leu Val Met Thr Gln Ser
 245 250 255
 Pro Ser Ser Leu Thr Val Thr Ala Gly Glu Lys Val Thr Met Ser Cys
 260 265 270
 Lys Ser Ser Gln Ser Leu Leu Asn Ser Gly Asn Gln Lys Asn Tyr Leu
 275 280 285
 Thr Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr
 290 295 300
 Trp Ala Ser Thr Arg Glu Ser Gly Val Pro Asp Arg Phe Thr Gly Ser
 305 310 315 320
 Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Val Gln Ala Glu
 325 330 335
 Asp Leu Ala Val Tyr Tyr Cys Gln Asn Asp Tyr Ser Tyr Pro Leu Thr
 340 345 350
 Phe Gly Ala Gly Thr Lys Leu Glu Ile Lys Gly Gly Gly Gly Ser Gly
 355 360 365
 Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Leu Glu Gln
 370 375 380
 Ser Gly Ala Glu Leu Val Arg Pro Gly Thr Ser Val Lys Ile Ser Cys
 385 390 395 400
 Lys Ala Ser Gly Tyr Ala Phe Thr Asn Tyr Trp Leu Gly Trp Val Lys
 405 410 415

40

Gln Arg Pro Gly His Gly Leu Glu Trp Ile Gly Asp Ile Phe Pro Gly
420 425 430

Ser Gly Asn Ile His Tyr Asn Glu Lys Phe Lys Gly Lys Ala Thr Leu
435 440 445

Thr Ala Asp Lys Ser Ser Ser Thr Ala Tyr Met Gln Leu Ser Ser Leu
450 455 460

Thr Phe Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg Leu Arg Asn Trp
465 470 475 480

Asp Glu Pro Met Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser
485 490 495

Ser

<210> 40

<211> 35

<212> DNA

<213> artificial sequence

<220>

<223> DI anti-CD3 K52VHBsrGI

<400> 40
aggtgtacac tccgacgtcc aactggtgca gtcag

35

<210> 41

<211> 30

<212> DNA

<213> artificial sequence

<220>

<223> DI anti-CD3 52VLBspEI

<400> 41
aatccggatt tgatctccac cttggtcccg

30

<210> 42

<211> 51

<212> DNA

<213> artificial sequence

<220>

<223> 4-7 VH GS15 FOR

<400> 42

ggcggcggcg gctccggtgg tgggtggttct gaggtgcagc tgctcgagca g

51

<210> 43

<211> 53

<212> DNA

<213> artificial sequence

<220>

<223> 4-7 VH SalI REV

<400> 43

ttttaagtcg acctaattgat gatgatgatg atgtgaggag acggtgaccg tgg

53

<210> 44

<211> 49

<212> DNA

<213> artificial sequence

<220>

<223> 510VLBspEI

<400> 44

ctgaaatccg gaggtggtgg atccgagctc gtgatgacac agtctccat

49

<210> 45

<211> 53

<212> DNA

<213> artificial sequence

<220>

<223> 510VLGS15REV

<400> 45

ggagccgccc ccgccagaac caccaccacc tttgatctca agcttggtcc cag

53

<210> 46

<211> 49

<212> DNA

<213> artificial sequence

<220>

<223> 510VHGS15

<400> 46
ggcggcggcg gctccggtgg tgggtggttct gaggtgcagc tgctcgagc

49

<210> 47

<211> 53

<212> DNA

<213> artificial sequence

<220>

<223> 510VHSalIREV

<400> 47
ttttaagtcg acctaatgat gatgatgatg atgtgaggag acggtgaccg tgg

53

<210> 48

<211> 1518

<212> DNA

<213> artificial sequence

<220>

<223> 3-1(VL-VH)xanti-CD3(VH(5)-VL(2))

<400> 48
atgggatgga gctgtatcat cctcttcttg gtagcaacag ctacaggtgt acactccgag 60
ctcgtcatga cccagtctcc atcttatctt gctgcatctc ctggagaaac cattactatt 120
aattgcaggg caagtaagag cattagcaaa tatttagcct ggtatcaaga gaaacctggg 180
aaaactaata agcttcttat ctactctgga tccactttgc aatctggaat tccatcaagg 240
ttcagtggca gtggatctgg tacagatttc actctcacca tcagtagcct ggagcctgaa 300
gattttgcaa tgtattactg tcaacagcat aatgaatatc cgtacacggt cggagggggg 360
accaagcttg agatcaaagg tgggtggtggt tctggcggcg gcggctccgg tgggtggtggt 420
tctgaggtgc agctgctcga gcagtctgga gctgagctgg tgaaacctgg ggcctcagtg 480
aagatatcct gcaaggcttc tggatacgcc ttcactaact actggctagg ttgggtaaag 540
cagaggcctg gacatggact tgagtggatt ggagatcttt tccctggaag tggtaatact 600
cactacaatg agaggttcag gggcaaagcc aactgactg cagacaaatc ctcgagcaca 660
gcctttatgc agctcagtag cctgacatct gaggactctg ctgtctatct ctgtgcaaga 720

ttgaggaact gggacgagggc tatggactac tggggccaag ggaccacggt caccgtctcc 780
 tccggagggtg gtggctccga cgtccaactg gtgcagtcag gggctgaagt gaaaaaacct 840
 ggggcctcag tgaagggtgtc ctgcaagggt tctggctaca cctttactag gtacacgatg 900
 cactgggtaa ggcaggcacc tggacagggt ctggaatgga ttggatacat taatcctagc 960
 cgtgggttata ctaattacgc agacagcgtc aaggggccgct tcacaatcac tacagacaaa 1020
 tccaccagca cagcctacat ggaactgagc agcctgcgtt ctgaggacac tgcaacctat 1080
 tactgtgcaa gatattatga tgatcattac tgccttgact actggggcca aggcaccacg 1140
 gtcaccgtct cctcaggcga aggtactagt actgggttctg gaggttcagg tggagcagac 1200
 gacattgtac tgaccagtc tccagcaact ctgtctctgt ctccagggga gcgtgccacc 1260
 ctgagctgca gagccagtca aagtgtaagt tacatgaact ggtaccagca gaagccgggc 1320
 aaggcaccca aaagatggat ttatgacaca tccaaagtgg cttctggagt ccctgctcgc 1380
 ttcagtggca gtgggtctgg gaccgactac tctctcacia tcaacagctt ggaggctgaa 1440
 gatgctgcca cttattactg ccaacagtgg agtagtaacc cgctcacgtt cggtggcggg 1500
 accaagggtg agatcaaa 1518

<210> 49

<211> 506

<212> PRT

<213> artificial sequence

<220>

<223> 3-1(VL-VH)xanti-CD3(VH(5)-VL(2))

<400> 49

Met Gly Trp Ser Cys Ile Ile Leu Phe Leu Val Ala Thr Ala Thr Gly
 1 5 10 15

Val His Ser Glu Leu Val Met Thr Gln Ser Pro Ser Tyr Leu Ala Ala
 20 25 30

Ser Pro Gly Glu Thr Ile Thr Ile Asn Cys Arg Ala Ser Lys Ser Ile
 35 40 45

Ser Lys Tyr Leu Ala Trp Tyr Gln Glu Lys Pro Gly Lys Thr Asn Lys
 50 55 60

Leu Leu Ile Tyr Ser Gly Ser Thr Leu Gln Ser Gly Ile Pro Ser Arg
 65 70 75 80

Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser
 85 90 95

Leu Glu Pro Glu Asp Phe Ala Met Tyr Tyr Cys Gln Gln His Asn Glu
 100 105 110

Tyr Pro Tyr Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Gly Gly
 115 120 125

Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Val Gln
 130 135 140

Leu Leu Glu Gln Ser Gly Ala Glu Leu Val Lys Pro Gly Ala Ser Val
 145 150 155 160

Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Thr Asn Tyr Trp Leu
 165 170 175

Gly Trp Val Lys Gln Arg Pro Gly His Gly Leu Glu Trp Ile Gly Asp
 180 185 190

Leu Phe Pro Gly Ser Gly Asn Thr His Tyr Asn Glu Arg Phe Arg Gly
 195 200 205

Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala Phe Met Gln
 210 215 220

Leu Ser Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg
 225 230 235 240

Leu Arg Asn Trp Asp Glu Ala Met Asp Tyr Trp Gly Gln Gly Thr Thr
 245 250 255

Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp Val Gln Leu Val Gln
 260 265 270

Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys
 275 280 285

Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp Val Arg
 290 295 300

Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn Pro Ser
 305 310 315 320

Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile
 325 330 335

Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser Ser Leu
 340 345 350

Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys Ala Arg Tyr Tyr Asp Asp
 355 360 365

His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser
370 375 380

Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly Gly Ser Gly Gly Ala Asp
385 390 395 400

Asp Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
405 410 415

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Tyr Met
420 425 430

Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr
435 440 445

Asp Thr Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
450 455 460

Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu
465 470 475 480

Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr
485 490 495

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
500 505

<210> 50

<211> 60

<212> DNA

<213> artificial sequence

<220>

<223> Me83

<400> 50

ggttctggcg gcggcggctc cggtggtggt ggttctgagg tgcagctgct cgacagtctg

60

<210> 51

<211> 41

<212> DNA

<213> artificial sequence

<220>

<223> Me84

<400> 51

gtgctccgga ggagacggtg accgtggtcc cttggcccca g 46 41

<210> 52
<211> 53
<212> DNA
<213> artificial sequence

<220>
<223> Me90
<400> 52
ccggagccgc cgccgccaga accaccacca cctttgatct caagcttggt ccc 53

<210> 53
<211> 52
<212> DNA
<213> artificial sequence

<220>
<223> Me91a
<400> 53
ggattgtaca ctccgagctc gtcattgaccc agtctccatc ttattcttgc gc 52

<210> 54
<211> 1560
<212> DNA
<213> artificial sequence

<220>
<223> 3-5(VL-VH)xanti-CD3 (VH(5)-VL(2))
<400> 54
atgggatgga gctgtatcat cctcttcttg gtagcaacag ctacaggtgt acactccgcg 60
cgcgagctcg tgatgacca gactccactc tccctgcctg tcagtcttgg agatcaagcc 120
tccatctctt gcagatctag tcagagcctt gtacacagta atggaaacac ctattttacat 180
tggtacctgc agaagccagg ccagtctcca aagctcctga tctacaaagt ttccaaccga 240
ttttctgggg tcccagacag gttcagtggc agtggatcag ggacagattt cacactcaag 300
atcagcagag tggaggctga ggatctggga gtttattttct gctctcaaag tacacatggt 360
ccgtacacgt tcggaggggg gaccaagctt gagatcaaag gtggtggtgg ttctggcggc 420
ggcggctccg gtggtggtgg ttctgaggtg cagctgctcg agcagtctgg agctgagctg 480

gtaaggcctg ggacttcagt gaagctgtcc tgcaaggctt ctggctacac cttcacaagc 540
 tatggtttaa gctgggtgaa gcagagaact ggacagggcc ttgagtggat tggagagggtt 600
 taccctagaa ttggtaatgc ttactacaat gagaagttca agggcaaggc cacactgact 660
 gcagacaaat cctccagcac agcgtccatg gagctccgca gcctgacatc tgaggactct 720
 gcggtctatt tctgtgcaag acggggatcc tacggtagta actacgactg gtacttcgat 780
 gtctggggcc aagggaccac ggtcacccgtc tcctccggag gtggtggctc cgacgtccaa 840
 ctggtgcagt caggggctga agtgaaaaaa cctggggcct cagtgaagggt gtcctgcaag 900
 gcttctggct acacctttac taggtacacg atgcactggg taaggcaggc acctggacag 960
 ggtctggaat ggattggata cattaatcct agccgtgggtt atactaatta cgcagacagc 1020
 gtcaagggcc gcttcacaat cactacagac aaatccacca gcacagccta catggaactg 1080
 agcagcctgc gttctgagga cactgcaacc tattactgtg caagatatta tgatgatcat 1140
 tactgccttg actactgggg ccaaggcacc acggtcaccg tctcctcagg cgaagggtact 1200
 agtactgggt ctggtggaag tggagggttca ggtggagcag acgacattgt actgaccag 1260
 tctccagcaa ctctgtctct gtctccaggg gagcgtgcca ccctgagctg cagagccagt 1320
 caaagtgtaa gttacatgaa ctggtaccag cagaagccgg gcaaggcacc caaaagatgg 1380
 atttatgaca catccaaagt ggcttctgga gtccctgctc gcttcagtgg cagtgggtct 1440
 gggaccgact actctctcac aatcaacagc ttggaggctg aagatgctgc cacttattac 1500
 tgccaacagt ggagtagtaa cccgctcacg ttcggtggcg ggaccaagggt ggagatcaaa 1560

<210> 55

<211> 520

<212> PRT

<213> artificial sequence

<220>

<223> 3-5(VL-VH)xanti-CD3 (VH(5)-VL(2))

<400> 55

Met Gly Trp Ser Cys Ile Ile Leu Phe Leu Val Ala Thr Ala Thr Gly
 1 5 10 15

Val His Ser Ala Arg Glu Leu Val Met Thr Gln Thr Pro Leu Ser Leu
 20 25 30

Pro Val Ser Leu Gly Asp Gln Ala Ser Ile Ser Cys Arg Ser Ser Gln
 35 40 45

Ser Leu Val His Ser Asn Gly Asn Thr Tyr Leu His Trp Tyr Leu Gln
 50 55 60

Lys Pro Gly Gln Ser Pro Lys Leu Leu Ile Tyr Lys Val Ser Asn Arg
65 70 75 80

Phe Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp
85 90 95

Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu Asp Leu Gly Val Tyr
100 105 110

Phe Cys Ser Gln Ser Thr His Val Pro Tyr Thr Phe Gly Gly Gly Thr
115 120 125

Lys Leu Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
130 135 140

Gly Gly Gly Ser Glu Val Gln Leu Leu Glu Gln Ser Gly Ala Glu Leu
145 150 155 160

Val Arg Pro Gly Thr Ser Val Lys Leu Ser Cys Lys Ala Ser Gly Tyr
165 170 175

Thr Phe Thr Ser Tyr Gly Leu Ser Trp Val Lys Gln Arg Thr Gly Gln
180 185 190

Gly Leu Glu Trp Ile Gly Glu Val Tyr Pro Arg Ile Gly Asn Ala Tyr
195 200 205

Tyr Asn Glu Lys Phe Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser
210 215 220

Ser Ser Thr Ala Ser Met Glu Leu Arg Ser Leu Thr Ser Glu Asp Ser
225 230 235 240

Ala Val Tyr Phe Cys Ala Arg Arg Gly Ser Tyr Gly Ser Asn Tyr Asp
245 250 255

Trp Tyr Phe Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
260 265 270

Gly Gly Gly Gly Ser Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val
275 280 285

Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr
290 295 300

Thr Phe Thr Arg Tyr Thr Met His Trp Val Arg Gln Ala Pro Gly Gln
305 310 315 320

Gly Leu Glu Trp Ile Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn
325 330 335

Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr⁴⁹ Ile Thr Thr Asp Lys Ser
 340 345 350
 Thr Ser Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr
 355 360 365
 Ala Thr Tyr Tyr Cys Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp
 370 375 380
 Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Glu Gly Thr
 385 390 395 400
 Ser Thr Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile
 405 410 415
 Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg
 420 425 430
 Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Tyr Met Asn Trp
 435 440 445
 Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr
 450 455 460
 Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser
 465 470 475 480
 Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala
 485 490 495
 Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly
 500 505 510
 Gly Gly Thr Lys Val Glu Ile Lys
 515 520

<210> 56

<211> 40

<212> DNA

<213> artificial sequence

<220>

<223> Me81

<400> 56

ggatgcgcgc gagctcgtga tgaccagac tccactctcc

<210> 57

<211> 1545

<212> DNA

<213> artificial sequence

<220>

<223> 4-1(VL-VH)xanti-CD3(VH(5)-VL(2))

<400> 57
 atgggatgga gctgtatcat cctcttcttg gtagcaacag ctacagggtgt acactccgag 60
 ctctgtgatga cacagtctcc atcctccctg agtgtgtcag caggagagaa ggtcactatg 120
 agctgcaagt ccagtcagag tctgttaaac agtggaatc aaaagaacta cttggcctgg 180
 taccagcaga aaccagggca gcctcctaaa ctgttgatct acggggcatc cactagggaa 240
 tctgggggtcc ctgatcgctt cacaggcagt ggatctggaa cagatttcac tctcaccatc 300
 agcagtgtgc aggctgaaga cctggcagtt tattactgtc agaatgatta tagttatccg 360
 tacacgttcg gaggggggac caagcttgag atcaaagggtg gtggtggttc tggcggcggc 420
 ggctccggtg gtggtggttc tgagggtgcag ctgctcgagc agtctggagc tgagctggta 480
 aggctggga cttcagtga gatatcctgc aaggcttctg gatacgcctt cactaactac 540
 tggctagggtt gggtaagca gaggcctgga catggacttg aatgggttgg agatattttc 600
 cctggaagtg gtaatgctca ctacaatgag aagttcaagg gcaaagccac actgactgca 660
 gacaagtcct cgtacacagc ctatatgcag ctacagtagcc tgacatctga ggactctgct 720
 gtctatttct gtgcaagatt gcggaactgg gacgaggcta tggactactg gggccaaggg 780
 accacggtca ccgtctcttc cggagggtgg ggctccgacg tccaactggg gcagtcaggg 840
 gctgaagtga aaaaacctgg ggcctcagtg aagggtgtcct gcaaggcttc tggctacacc 900
 ttactaggt acacgatgca ctgggtaagg caggcacctg gacagggtct ggaatggatt 960
 ggatacatta atcctagccg tggttatact aattacgcag acagcgtcaa gggccgcttc 1020
 acaatcacta cagacaaatc caccagcaca gcctacatgg aactgagcag cctgcgttct 1080
 gaggacactg caacctatta ctgtgcaaga tattatgatg atcattactg ccttgactac 1140
 tggggccaag gcaccacggt caccgtctcc tcaggcgaag gtactagtagc tgggttctggt 1200
 ggaagtggag gttcagggtg agcagacgac attgtactga ccagtcctcc agcaactctg 1260
 tctctgtctc caggggagcg tgccaccctg agctgcagag ccagtcaaag tgtaagttac 1320
 atgaactggg accagcagaa gccgggcaag gcacccaaaa gatggattta tgacacatcc 1380
 aaagtggctt ctggagtccc tgctcgcttc agtggcagtg ggtctgggac cgactactct 1440
 ctcaaatca acagcttgga ggctgaagat gctgccactt attactgcca acagtggagt 1500
 agtaaccgcg tcacgttcgg tggcgggacc aagggtggaga tcaaa 1545

<210> 58

<211> 515

<212> PRT

<213> artificial sequence

<220>

<223> 4-1(VL-VH)xanti-CD3(VH(5)-VL(2))

<400> 58

Met Gly Trp Ser Cys Ile Ile Leu Phe Leu Val Ala Thr Ala Thr Gly
 1 5 10 15

Val His Ser Glu Leu Val Met Thr Gln Ser Pro Ser Ser Leu Ser Val
 20 25 30

Ser Ala Gly Glu Lys Val Thr Met Ser Cys Lys Ser Ser Gln Ser Leu
 35 40 45

Leu Asn Ser Gly Asn Gln Lys Asn Tyr Leu Ala Trp Tyr Gln Gln Lys
 50 55 60

Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr Gly Ala Ser Thr Arg Glu
 65 70 75 80

Ser Gly Val Pro Asp Arg Phe Thr Gly Ser Gly Ser Gly Thr Asp Phe
 85 90 95

Thr Leu Thr Ile Ser Ser Val Gln Ala Glu Asp Leu Ala Val Tyr Tyr
 100 105 110

Cys Gln Asn Asp Tyr Ser Tyr Pro Tyr Thr Phe Gly Gly Gly Thr Lys
 115 120 125

Leu Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
 130 135 140

Gly Gly Ser Glu Val Gln Leu Leu Glu Gln Ser Gly Ala Glu Leu Val
 145 150 155 160

Arg Pro Gly Thr Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala
 165 170 175

Phe Thr Asn Tyr Trp Leu Gly Trp Val Lys Gln Arg Pro Gly His Gly
 180 185 190

Leu Glu Trp Val Gly Asp Ile Phe Pro Gly Ser Gly Asn Ala His Tyr
 195 200 205

Asn Glu Lys Phe Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser
 210 215 220

Tyr Thr Ala Tyr Met Gln Leu Ser Ser Leu Thr Ser Glu Asp Ser Ala

225		230		52 235		240
Val Tyr Phe Cys	Ala 245	Arg Leu Arg Asn	Trp 250	Asp Glu Ala Met	Asp 255	Tyr
Trp Gly Gln	Gly 260	Thr Thr Val Thr	Val 265	Ser Ser Gly Gly	Gly 270	Gly Ser
Asp Val	Gln 275	Leu Val Gln Ser	Gly 280	Ala Glu Val Lys	Lys 285	Pro Gly Ala
Ser Val	Lys 290	Val Ser Cys	Lys 295	Ala Ser Gly Tyr	Thr 300	Phe Thr Arg Tyr
Thr Met His Trp	Val 310	Arg Gln Ala Pro	Gly 315	Gln Gly Leu Glu	Trp 320	Ile
Gly Tyr Ile Asn	Pro 325	Ser Arg Gly Tyr	Thr 330	Asn Tyr Ala Asp	Ser 335	Val
Lys Gly Arg	Phe 340	Thr Ile Thr Thr	Asp 345	Lys Ser Thr Ser	Thr 350	Ala Tyr
Met Glu	Leu 355	Ser Ser Leu Arg	Ser 360	Glu Asp Thr Ala	Thr 365	Tyr Tyr Cys
Ala Arg Tyr Tyr	Asp 370	Asp His Tyr Cys	Leu 375	Asp Tyr Trp Gly	Gln 380	Gly
Thr Thr Val Thr	Val 385	Ser 390	Ser Gly Glu Gly	Thr 395	Ser Thr Gly Ser	Gly 400
Gly Ser Gly Gly	Ser 405	Gly Gly Ala Asp	Asp 410	Ile Val Leu Thr	Gln 415	Ser
Pro Ala Thr	Leu 420	Ser Leu Ser Pro	Gly 425	Glu Arg Ala Thr	Leu 430	Ser Cys
Arg Ala Ser	Gln 435	Ser Val Ser Tyr	Met 440	Asn Trp Tyr Gln	Gln 445	Lys Pro
Gly Lys Ala Pro	Lys 450	Arg Trp Ile Tyr	Asp 455	Thr Ser Lys Val	Ala 460	Ser
Gly Val Pro Ala	Arg 465	Phe Ser Gly Ser	Gly 470	Ser Gly Thr Asp	Tyr 475	Ser
Leu Thr Ile Asn	Ser 485	Leu Glu Ala Glu	Asp 490	Ala Ala Thr Tyr	Tyr 495	Cys
Gln Gln Trp Ser	Ser 500	Asn Pro Leu Thr	Phe 505	Gly Gly Gly Thr	Lys 510	Val

Glu Ile Lys
515

<210> 59

<211> 44

<212> DNA

<213> artificial sequence

<220>

<223> Me92a

<400> 59

ggattgtaca ctccgagctc gtgatgacac agtctccatc ctcc

44

<210> 60

<211> 1560

<212> DNA

<213> artificial sequence

<220>

<223> 4-7(VL-VH)xanti-CD3(VH(5)-VL(2))

<400> 60

atgggatgga gctgtatcat cctcttcttg gtagcaacag ctacaggtgt acactccgcg	60
cgcgagctcg tgatgaccca gactccactc tccctgcctg tcagtcttgg agatcaagcc	120
tccatctctt gcagatctag tcagagcctt gtacacagta atggaaacac ctattttacat	180
tggtacctgc agaagccagg ccagtctcca aagctcctga tctacaaagt ttccaaccga	240
ttttctgggg tcccagacag gttcagtggc agtggatcag ggacagattt cacactcaag	300
atcagcagag tggaggctga ggatctggga gtttatttct gctctcaaag tacacatggt	360
ccgtacacgt tcggaggggg gaccaagctt gagatcaaag gtggtggtgg ttctggcggc	420
ggcggctccg gtggtggtgg ttctgaggtg cagctgctcg agcagtctgg agctgagctg	480
gcgaggcctg gggcttcagt gaagctgtcc tgcaaggctt ctggctacac cttcaciaaac	540
tatggtttaa gctgggtgaa gcagaggcct ggacaggctc ttgagtggat tggagagggt	600
tatcctagaa ttggtaatgc ttactacaat gagaagttca agggcaaggc cacactgact	660
gcagacaaat cctccagcac agcgtccatg gagctccgca gcctgacctc tgaggactct	720
gcggtctatt tctgtgcaag acggggatcc tacgatacta actacgactg gtacttcgat	780
gtctggggcc aagggaaccac ggtcaccgtc tcctccggag gtggtggctc cgacgtccaa	840
ctggtgcagt caggggctga agtgaaaaaa cctggggcct cagtgaagggt gtcctgcaag	900

54

gcttctggct acacctttac taggtacacg atgcactggg taaggcaggc acctggacag	960
ggctctggaat ggattggata cattaatcct agccgtgggt atactaatta cgcagacagc	1020
gtcaagggcc gcttcacaat cactacagac aaatccacca gcacagccta catggaactg	1080
agcagcctgc gttctgagga cactgcaacc tattactgtg caagatatta tgatgatcat	1140
tactgccttg actactgggg ccaaggcacc acggtcaccg tctcctcagg cgaagggtact	1200
agtactgggt ctggtggaag tggagggttca ggtggagcag acgacattgt actgacccag	1260
tctccagcaa ctctgtctct gtctccaggg gagcgtgcc aacctgagctg cagagccagt	1320
caaagtgtaa gttacatgaa ctggtaccag cagaagccgg gcaaggcacc caaaagatgg	1380
atttatgaca catccaaagt ggcttctgga gtccctgctc gcttcagtgg cagtgggtct	1440
gggaccgact actctctcac aatcaacagc ttggaggctg aagatgctgc cacttattac	1500
tgccaacagt ggagtagtaa cccgctcacg ttcggtggcg ggaccaaggt ggagatcaaa	1560

<210> 61

<211> 520

<212> PRT

<213> artificial sequence

<220>

<223> 4-7(VL-VH)xanti-CD3(VH(5)-VL(2))

<400> 61

Met Gly Trp Ser Cys Ile Ile Leu Phe Leu Val Ala Thr Ala Thr Gly
1 5 10 15

Val His Ser Ala Arg Glu Leu Val Met Thr Gln Thr Pro Leu Ser Leu
20 25 30

Pro Val Ser Leu Gly Asp Gln Ala Ser Ile Ser Cys Arg Ser Ser Gln
35 40 45

Ser Leu Val His Ser Asn Gly Asn Thr Tyr Leu His Trp Tyr Leu Gln
50 55 60

Lys Pro Gly Gln Ser Pro Lys Leu Leu Ile Tyr Lys Val Ser Asn Arg
65 70 75 80

Phe Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp
85 90 95

Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu Asp Leu Gly Val Tyr
100 105 110

Phe Cys Ser Gln Ser Thr His Val Pro Tyr Thr Phe Gly Gly Gly Thr
115 120 125

Lys Leu Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
 130 135 140
 Gly Gly Gly Ser Glu Val Gln Leu Leu Glu Gln Ser Gly Ala Glu Leu
 145 150 155 160
 Ala Arg Pro Gly Ala Ser Val Lys Leu Ser Cys Lys Ala Ser Gly Tyr
 165 170 175
 Thr Phe Thr Asn Tyr Gly Leu Ser Trp Val Lys Gln Arg Pro Gly Gln
 180 185 190
 Val Leu Glu Trp Ile Gly Glu Val Tyr Pro Arg Ile Gly Asn Ala Tyr
 195 200 205
 Tyr Asn Glu Lys Phe Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser
 210 215 220
 Ser Ser Thr Ala Ser Met Glu Leu Arg Ser Leu Thr Ser Glu Asp Ser
 225 230 235 240
 Ala Val Tyr Phe Cys Ala Arg Arg Gly Ser Tyr Asp Thr Asn Tyr Asp
 245 250 255
 Trp Tyr Phe Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
 260 265 270
 Gly Gly Gly Gly Ser Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val
 275 280 285
 Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr
 290 295 300
 Thr Phe Thr Arg Tyr Thr Met His Trp Val Arg Gln Ala Pro Gly Gln
 305 310 315 320
 Gly Leu Glu Trp Ile Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn
 325 330 335
 Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Thr Thr Asp Lys Ser
 340 345 350
 Thr Ser Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr
 355 360 365
 Ala Thr Tyr Tyr Cys Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp
 370 375 380
 Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Glu Gly Thr
 385 390 395 400

Ser Thr Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile
 405 410 415

Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg
 420 425 430

Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Tyr Met Asn Trp
 435 440 445

Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr
 450 455 460

Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser
 465 470 475 480

Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala
 485 490 495

Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly
 500 505 510

Gly Gly Thr Lys Val Glu Ile Lys
 515 520

<210> 62

<211> 1545

<212> DNA

<213> artificial sequence

<220>

<223> 5-10(VL-VH)xanti-CD3(VH(5)-VL(2))

<400> 62
 atgggatgga gctgtatcat cctcttcttg gtagcaacag ctacaggtgt acactccgag 60
 ctcgtgatga cacagtctcc atcctccctg actgtgacag caggagagaa ggtcactatg 120
 agctgcaagt ccagtcagag tctgttaaac agtggaaatc aaaagaacta cttgacctgg 180
 taccagcaga aaccagggca gcctcctaaa ctgttgatct actgggcatc cactagggaa 240
 tctgggggtcc ctgatcgctt cacaggcagt ggatctggaa cagatttcac tctcaccatc 300
 agcagtgtgc aggctgaaga cctggcagtt tattactgtc agaatgatta tagttatccg 360
 ctcacgttcg gtgctgggac caagcttgag atcaaagggtg gtggtgggttc tggcggcggc 420
 ggctccggtg gtggtgggttc tgaggtgcag ctgctcgagc agtctggagc tgagctggta 480
 aggcctggga cttcagtgaa gatatcctgc aaggcttctg gatacgctt cactaactac 540
 tggctaggtt gggtaaagca gaggcctgga catggacttg agtggattgg agatattttc 600
 cctggaagtg gtaatatcca ctacaatgag aagttcaagg gcaaagccac actgactgca 660

gacaaatctt cgagcacagc ctatatgcag cttagtagcc tgacatttga ggactctgct 720
 gtctatttct gtgcaagact gaggaactgg gacgagccta tggactactg gggccaaggg 780
 accacgggtca ccgtctcctc cggaggtggg ggctccgacg tccaactggg gcagtcaggg 840
 gctgaagtga aaaaacctgg ggcctcagtg aaggtgtcct gcaaggcttc tggctacacc 900
 tttagtaggt acacgatgca ctgggtaagg caggcacctg gacaggggtct ggaatggatt 960
 ggatacatta atcctagccg tggttatact aattacgcag acagcgtcaa gggccgcttc 1020
 acaatcacta cagacaaatc caccagcaca gcctacatgg aactgagcag cctgcgttct 1080
 gaggacactg caacctatta ctgtgcaaga tattatgatg atcattactg ccttgactac 1140
 tggggccaag gcaccacggg caccgtctcc tcaggcgaag gtactagtac tggttctggg 1200
 ggaagtggag gttcaggtgg agcagacgac attgtactga cccagtctcc agcaactctg 1260
 tctctgtctc caggggagcg tgccaccctg agctgcagag ccagtcaaag tgtaagttac 1320
 atgaactggg accagcagaa gccgggcaag gcacccaaaa gatggattta tgacacatcc 1380
 aaagtggctt ctggagtccc tgctcgcttc agtggcagtg ggtctgggac cgactactct 1440
 ctcaaatca acagcttgga ggctgaagat gctgccactt attactgcca acagtggagt 1500
 agtaaccgc tcacgttcgg tggcgggacc aaggtggaga tcaaa 1545

<210> 63

<211> 515

<212> PRT

<213> artificial sequence

<220>

<223> 5-10(VL-VH)xanti-CD3(VH(5)-VL(2))

<400> 63

Met Gly Trp Ser Cys Ile Ile Leu Phe Leu Val Ala Thr Ala Thr Gly
1 5 10 15

Val His Ser Glu Leu Val Met Thr Gln Ser Pro Ser Ser Leu Thr Val
20 25 30

Thr Ala Gly Glu Lys Val Thr Met Ser Cys Lys Ser Ser Gln Ser Leu
35 40 45

Leu Asn Ser Gly Asn Gln Lys Asn Tyr Leu Thr Trp Tyr Gln Gln Lys
50 55 60

Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr Trp Ala Ser Thr Arg Glu
65 70 75 80

Ser Gly Val Pro Asp Arg Phe Thr Gly Ser Gly Ser Gly Thr Asp Phe

85

90 58

95

Thr Leu Thr Ile Ser Ser Val Gln Ala Glu Asp Leu Ala Val Tyr Tyr
100 105 110

Cys Gln Asn Asp Tyr Ser Tyr Pro Leu Thr Phe Gly Ala Gly Thr Lys
115 120 125

Leu Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
130 135 140

Gly Gly Ser Glu Val Gln Leu Leu Glu Gln Ser Gly Ala Glu Leu Val
145 150 155 160

Arg Pro Gly Thr Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala
165 170 175

Phe Thr Asn Tyr Trp Leu Gly Trp Val Lys Gln Arg Pro Gly His Gly
180 185 190

Leu Glu Trp Ile Gly Asp Ile Phe Pro Gly Ser Gly Asn Ile His Tyr
195 200 205

Asn Glu Lys Phe Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser
210 215 220

Ser Thr Ala Tyr Met Gln Leu Ser Ser Leu Thr Phe Glu Asp Ser Ala
225 230 235 240

Val Tyr Phe Cys Ala Arg Leu Arg Asn Trp Asp Glu Pro Met Asp Tyr
245 250 255

Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser
260 265 270

Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
275 280 285

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr
290 295 300

Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
305 310 315 320

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val
325 330 335

Lys Gly Arg Phe Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr
340 345 350

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys
355 360 365

Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
370 375 380

Thr Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly
385 390 395 400

Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Val Leu Thr Gln Ser
405 410 415

Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys
420 425 430

Arg Ala Ser Gln Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro
435 440 445

Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser
450 455 460

Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser
465 470 475 480

Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys
485 490 495

Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
500 505 510

Glu Ile Lys
515

<210> 64

<211> 1500

<212> DNA

<213> artificial sequence

<220>

<223> VH5/VL2x3-5

<400> 64

gacgtccaac tgggtgcagtc aggggctgaa gtgaaaaaac ctggggcctc agtgaagggtg	60
tcctgcaagg cttctggcta cacctttact aggtacacga tgcactgggt aaggcaggca	120
cctggacagg gtctggaatg gattggatac attaatccta gccgtgggtta tactaattac	180
gcagacagcg tcaagggccg cttcacaatc actacagaca aatccaccag cacagcctac	240
atggaactga gcagcctgcg ttctgaggac actgcaacct attactgtgc aagatattat	300
gatgatcatt actgccttga ctactggggc caaggcacca cggtcaccgt ctctcaggc	360

60

gaaggtacta gtactggttc tgggtggaagt ggaggttcag gtggagcaga cgacattgta	420
ctgacccagt ctccagcaac tctgtctctg tctccagggg agcgtgccac cctgagctgc	480
agagccagtc aaagtgtaag ttacatgaac tggtagcagc agaagccggg caaggcaccc	540
aaaagatgga tttatgacac atccaaagtg gcttctggag tccctgctcg cttcagtggc	600
agtgggtctg ggaccgacta ctctctcaca atcaacagct tggaggctga agatgctgcc	660
acttattact gccaacagtg gagtagtaac ccgctcacgt tcggtggcgg gaccaagggtg	720
gagatcaaat ccggagggtg tggatccgag gtgcagctgc tcgagcagtc tggagctgag	780
ctggtaaagg ctgggacttc agtgaagctg tcctgcaagg cttctggcta caccttcaca	840
agctatggtt taagctgggt gaagcagaga actggacagg gccttgagtg gattggagag	900
gtttatccta gaattggtaa tgcttactac aatgagaagt tcaagggcaa ggccacactg	960
actgcagaca aatcctccag cacagcgtcc atggagctcc gcagcctgac atctgaggac	1020
tctgcggtct atttctgtgc aagacgggga tcctacggta gtaactacga ctggtacttc	1080
gatgtctggg gccaaaggac cacggtcacc gtctcctcag gtggtgggtg ttctggcggc	1140
ggcggctccg gtggtgggtg ttctgagctc gtgatgacc agactccact ctccctgcct	1200
gtcagtcttg gagatcaagc ctccatctct tgcagatcta gtcagagcct tgtacacagt	1260
aatggaaaca cctatttaca ttggtacctg cagaagccag gccagtctcc aaagctcctg	1320
atctacaaag tttccaaccg attttctggg gtcccagaca ggttcagtgg cagtggatca	1380
gggacagatt tcacactcaa gatcagcaga gtggaggctg aggatctggg agtttatttc	1440
tgctctcaaa gtacacatgt tccgtacacg ttcggagggg ggaccaagct tgagatcaaa	1500

<210> 65

<211> 500

<212> PRT

<213> artificial sequence

<220>

<223> VH5/VL2x3-5

<400> 65

Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr
20 25 30

Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr
 65 70 75 80
 Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys
 85 90 95
 Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
 100 105 110
 Thr Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly
 115 120 125
 Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Val Leu Thr Gln Ser
 130 135 140
 Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys
 145 150 155 160
 Arg Ala Ser Gln Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro
 165 170 175
 Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser
 180 185 190
 Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser
 195 200 205
 Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys
 210 215 220
 Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
 225 230 235 240
 Glu Ile Lys Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Leu Glu Gln
 245 250 255
 Ser Gly Ala Glu Leu Val Arg Pro Gly Thr Ser Val Lys Leu Ser Cys
 260 265 270
 Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr Gly Leu Ser Trp Val Lys
 275 280 285
 Gln Arg Thr Gly Gln Gly Leu Glu Trp Ile Gly Glu Val Tyr Pro Arg
 290 295 300
 Ile Gly Asn Ala Tyr Tyr Asn Glu Lys Phe Lys Gly Lys Ala Thr Leu
 305 310 315 320
 Thr Ala Asp Lys Ser Ser Ser Thr Ala Ser Met Glu Leu Arg Ser Leu
 325 330 335

Thr Ser Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg Arg Gly Ser Tyr
 340 345 350

Gly Ser Asn Tyr Asp Trp Tyr Phe Asp Val Trp Gly Gln Gly Thr Thr
 355 360 365

Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
 370 375 380

Gly Gly Gly Ser Glu Leu Val Met Thr Gln Thr Pro Leu Ser Leu Pro
 385 390 395 400

Val Ser Leu Gly Asp Gln Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser
 405 410 415

Leu Val His Ser Asn Gly Asn Thr Tyr Leu His Trp Tyr Leu Gln Lys
 420 425 430

Pro Gly Gln Ser Pro Lys Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe
 435 440 445

Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe
 450 455 460

Thr Leu Lys Ile Ser Arg Val Glu Ala Glu Asp Leu Gly Val Tyr Phe
 465 470 475 480

Cys Ser Gln Ser Thr His Val Pro Tyr Thr Phe Gly Gly Gly Thr Lys
 485 490 495

Leu Glu Ile Lys
 500

<210> 66

<211> 1491

<212> DNA

<213> artificial sequence

<220>

<223> VH5/VL2x4-1

<400> 66
 gacgtccaac tgggtgcagtc aggggctgaa gtgaaaaaac ctggggcctc agtgaagggtg 60
 tcctgcaagg cttctggcta cacctttact aggtacacga tgcactgggt aaggcaggca 120
 cctggacagg gtctggaatg gattggatac attaatccta gccgtgggta tactaattac 180
 gcagacagcg tcaagggccg cttcacaatc actacagaca aatccaccag cacagcctac 240
 atggaactga gcagcctgcg ttctgaggac actgcaacct attactgtgc aagatattat 300

gatgatcatt actgccttga ctactggggc caaggcacca cggtcaccgt ctcctcaggc 360
 gaaggtacta gtactgggttc tgggtggaagt ggagggttcag gtggagcaga cgacattgta 420
 ctgacccagt ctccagcaac tctgtctctg tctccagggg agcgtgccac cctgagctgc 480
 agagccagtc aaagtgtaag ttacatgaac tgggtaccagc agaagccggg caaggcaccc 540
 aaaagatgga tttatgacac atccaaagtg gcttctggag tccctgctcg cttcagtggc 600
 agtgggtctg ggaccgacta ctctctcaca atcaacagct tggaggctga agatgctgcc 660
 acttattact gccaacagtg gagtagtaac ccgctcacgt tcggtggcgg gaccaagggtg 720
 gagatcaaat ccggagggtg tggatccgag gtgcagctgc tcgagcagtc tggagctgag 780
 ctggtaaggc ctgggacttc agtgaagata tcctgcaagg cttctggata cgccttcact 840
 aactactggc taggttgggt taagcagagg cctggacatg gacttgaatg ggttggagat 900
 attttcctg gaagtggtaa tgctcactac aatgagaagt tcaagggcaa agccacactg 960
 actgcagaca agtcctcgta cacagcctat atgcagctca gtagcctgac atctgaggac 1020
 tctgctgtct atttctgtgc aagattgcgg aactgggacg aggctatgga ctactggggc 1080
 caagggacca cggtcaccgt ctcctcaggt ggtggtgggt ctggcggcgg cggctccggt 1140
 ggtggtgggt ctgagctcgt gatgacacag tctccatcct ccctgagtgt gtcagcagga 1200
 gagaagggtca ctatgagctg caagtccagt cagagtctgt taaacagtgg aaatcaaaag 1260
 aactacttgg cctggtacca gcagaaacca gggcagcctc ctaaactgtt gatctacggg 1320
 gcatccacta gggaatctgg ggtccctgat cgcttcacag gcagtggatc tggaacagat 1380
 ttcactctca ccatcagcag tgtgcaggct gaagacctgg cagtttatta ctgtcagaat 1440
 gattatagtt atccgtacac gttcggaggg gggaccaagc ttgagatcaa a 1491

<210> 67

<211> 497

<212> PRT

<213> artificial sequence

<220>

<223> VH5/VL2x4-1

<400> 67

Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
 1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr
 20 25 30

Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
 35 40 45

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val
 50 55 60

Lys Gly Arg Phe Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr
 65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys
 85 90 95

Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
 100 105 110

Thr Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly
 115 120 125

Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Val Leu Thr Gln Ser
 130 135 140

Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys
 145 150 155 160

Arg Ala Ser Gln Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro
 165 170 175

Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser
 180 185 190

Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser
 195 200 205

Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys
 210 215 220

Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
 225 230 235 240

Glu Ile Lys Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Leu Glu Gln
 245 250 255

Ser Gly Ala Glu Leu Val Arg Pro Gly Thr Ser Val Lys Ile Ser Cys
 260 265 270

Lys Ala Ser Gly Tyr Ala Phe Thr Asn Tyr Trp Leu Gly Trp Val Lys
 275 280 285

Gln Arg Pro Gly His Gly Leu Glu Trp Val Gly Asp Ile Phe Pro Gly
 290 295 300

Ser Gly Asn Ala His Tyr Asn Glu Lys Phe Lys Gly Lys Ala Thr Leu
 305 310 315 320

Thr Ala Asp Lys Ser Ser Tyr Thr Ala Tyr⁶⁵ Met Gln Leu Ser Ser Leu
 325 330 335
 Thr Ser Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg Leu Arg Asn Trp
 340 345 350
 Asp Glu Ala Met Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser
 355 360 365
 Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
 370 375 380
 Glu Leu Val Met Thr Gln Ser Pro Ser Ser Leu Ser Val Ser Ala Gly
 385 390 395 400
 Glu Lys Val Thr Met Ser Cys Lys Ser Ser Gln Ser Leu Leu Asn Ser
 405 410 415
 Gly Asn Gln Lys Asn Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln
 420 425 430
 Pro Pro Lys Leu Leu Ile Tyr Gly Ala Ser Thr Arg Glu Ser Gly Val
 435 440 445
 Pro Asp Arg Phe Thr Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
 450 455 460
 Ile Ser Ser Val Gln Ala Glu Asp Leu Ala Val Tyr Tyr Cys Gln Asn
 465 470 475 480
 Asp Tyr Ser Tyr Pro Tyr Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile
 485 490 495

Lys

<210> 68

<211> 18

<212> PRT

<213> artificial sequence

<220>

<223> non-deimmunized linker sequence

<400> 68

Val Glu Gly Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly
 1 5 10 15

Val Asp

<210> 69
 <211> 357
 <212> DNA
 <213> artificial sequence

<220>

<223> anti-CD3 VH2

<400> 69
 gacgtccaac tgggtgcagtc aggggctgaa gtgaaaaaac ctggggcctc agtgaagggtg 60
 tcctgcaagg cttctggcta caccgctact aggtacacga tgcactgggt aaggcaggca 120
 cctggacagg gtctggaatg gattggatac attaatccta gccgtgggta tactaattac 180
 gcacagaagt tgcagggccg cgtcacaatg actacagaca cttccaccag cacagcctac 240
 atggaactga gcagcctgcg ttctgaggac actgcaacct attactgtgc aagatattat 300
 gatgatcatt actgccttga ctactggggc caaggcacca cggtcaccgt ctcctca 357

<210> 70
 <211> 119
 <212> PRT
 <213> artificial sequence

<220>

<223> anti-CD3 VH2

<400> 70

Asp val Gln Leu val Gln Ser Gly Ala Glu val Lys Lys Pro Gly Ala
 1 5 10 15

Ser val Lys val Ser Cys Lys Ala Ser Gly Tyr Thr Ala Thr Arg Tyr
 20 25 30

Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
 35 40 45

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Gln Lys Leu
 50 55 60

Gln Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr
 65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys
 85 90 95

Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
 100 105 110

Thr Thr Val Thr Val Ser Ser
 115

<210> 71

<211> 357

<212> DNA

<213> artificial sequence

<220>

<223> anti-CD3 VH3

<400> 71

gacgtccaac	tggtgcagtc	aggggctgaa	gtgaaaaaac	ctggggcctc	agtgaagggtg	60
tcctgcaagg	cttctggcta	caccgctact	aggtacacga	tgcactgggt	aaggcaggca	120
cctggacagg	gtctggaatg	gattggatac	attaatccta	gccgtgggtta	tactaattac	180
gcacagaagt	tgcagggccg	cgtcacaatg	actacagaca	cttccaccag	cacagcctac	240
ctgcaaata	acagcctgaa	aactgaggac	actgcagtct	attactgtgc	aagatattat	300
gatgatcatt	actgccttga	ctactggggc	caaggcacca	cggtcaccgt	ctcctca	357

<210> 72

<211> 119

<212> PRT

<213> artificial sequence

<220>

<223> anti-CD3 VH3

<400> 72

Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
 1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Ala Thr Arg Tyr
 20 25 30

Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
 35 40 45

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Gln Lys Leu
 50 55 60

68

Gln Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Thr Val Thr Val Ser Ser
115

<210> 73

<211> 357

<212> DNA

<213> artificial sequence

<220>

<223> anti-CD3 VH5

<400> 73
gacgtccaac tgggtgcagtc aggggctgaa gtgaaaaaac ctggggcctc agtgaagggtg 60
tcctgcaagg cttctggcta cacctttact aggtacacga tgcactgggt aaggcaggca 120
cctggacagg gtctggaatg gattggatac attaatccta gccgtgggtta tactaattac 180
gcagacagcg tcaagggccg cttcacaatc actacagaca aatccaccag cacagcctac 240
atggaactga gcagcctgcg ttctgaggac actgcaacct attactgtgc aagatattat 300
gatgatcatt actgccttga ctactggggc caaggcacca cggtcaccgt ctcctca 357

<210> 74

<211> 119

<212> PRT

<213> artificial sequence

<220>

<223> anti-CD3 VH5

<400> 74

Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr
20 25 30

Thr Met His Trp Val Arg Gln Ala Pro Gly⁶⁹ Gln Gly Leu Glu Trp Ile
35 40 45

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys
85 90 95

Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Thr Val Thr Val Ser Ser
115

<210> 75

<211> 357

<212> DNA

<213> artificial sequence

<220>

<223> anti-CD3 VH7

<400> 75

gacgtccaac	tggtgcagtc	aggggctgaa	gtgaaaaaac	ctggggcctc	agtgaagggtg	60
tcctgcaagg	cttctggcta	cacctttact	aggtacacga	tgcactgggt	aaggcaggca	120
cctggacagg	gtctggaatg	gattggatac	attaatccta	gccgtgggta	tactaattac	180
aatcagaagt	tcaaggaccg	cgtcacaatc	actacagaca	aatccaccag	cacagcctac	240
atggaactga	gcagcctgcg	ttctgaggac	actgcagtct	attactgtgc	aagatattat	300
gatgatcatt	actgccttga	ctactggggc	caaggcacca	cggtcaccgt	ctcctca	357

<210> 76

<211> 119

<212> PRT

<213> artificial sequence

<220>

<223> anti-CD3 VH7

<400> 76

Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala

1 5 10 15 20 25 30 35 40 45 50 55 60 65 70 75 80 85 90 95 100 105 110 115

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr
Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe
Lys Asp Arg Val Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr
Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
Thr Thr Val Thr Val Ser Ser

<210>	77
<211>	318
<212>	DNA
<213>	artificial sequence

<220>

<223> anti-CD3 VL1

[illegible]

<210> 78

<211> 106

<212> PRT

<213> artificial sequence

<220>

<223> anti-CD3 VL1

<400> 78

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
 1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Ser Tyr Met
 20 25 30

Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr
 35 40 45

Asp Thr Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
 50 55 60

Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu
 65 70 75 80

Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr
 85 90 95

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
 100 105

<210> 79

<211> 318

<212> DNA

<213> artificial sequence

<220>

<223> anti-CD3 VL2

<400> 79

gacattgtac tgaccagtc tccagcaact ctgtctctgt ctccagggga gcgtgccacc	60
ctgagctgca gagccagtca aagtgttaagt tacatgaact ggtaccagca gaagccgggc	120
aaggcaccga aaagatggat ttatgacaca tccaaagtgg cttctggagt ccctgctcgc	180
ttcagtggca gtgggtctgg gaccgactac tctctcacia tcaacagctt ggaggctgaa	240
gatgctgcca cttattactg ccaacagtgg agtagtaacc cgctcacgtt cggtggcggg	300
accaaggtgg agatcaaa	318

<210> 80

<211> 106

<212> PRT

<213> artificial sequence

<220>

<223> anti-CD3 VL2

<400> 80

Asp Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
 1 5 10 15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Tyr Met
 20 25 30

Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr
 35 40 45

Asp Thr Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
 50 55 60

Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu
 65 70 75 80

Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr
 85 90 95

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
 100 105

<210> 81

<211> 318

<212> DNA

<213> artificial sequence

<220>

<223> anti-CD3 VL3

<400> 81
 gacattgtac tgaccagtc tccagcaact ctgtctctgt ctccagggga gcgtgccacc 60
 ctgacctgca gagccagttc aagtgttaagt tacatgaact ggtaccagca gaagccgggc 120
 aaggcaccca aaagatggat ttatgacaca tccaaagtgg cttctggagt ccctgctcgc 180
 ttcagtggca gtgggtctgg gaccgactac tctctcacia tcaacagctt ggaggctgaa 240
 gatgctgccca cttattactg ccaacagtgg agtagtaacc cgctcacgtt cggtggcggg 300
 accaaggtgg agatcaaa 318

<210> 82

<211> 106

<212> PRT

<213> artificial sequence

<220>

<223> anti-CD3 VL3

<400> 82

Asp Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
1 5 10 15

Glu Arg Ala Thr Leu Thr Cys Arg Ala Ser Ser Ser Val Ser Tyr Met
20 25 30

Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr
35 40 45

Asp Thr Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
50 55 60

Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu
65 70 75 80

Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr
85 90 95

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105

<210> 83

<211> 30

<212> DNA

<213> artificial sequence

<220>

<223> vH CDR1 anti-CD3 wt

<400> 83

ggctacacct ttactaggta cacgatgcac

30

<210> 84

<211> 10

<212> PRT

<213> artificial sequence

<220>

<223> vH CDR1 anti-CD3 wt

<400> 84

Gly Tyr Thr Phe Thr Arg Tyr Thr Met His
1 5 10

<210> 85

<211> 30

<212> DNA

<213> artificial sequence

<220>

<223> vH CDR1 VH2,3

<400> 85
ggctacaccg ctactaggta cacgatgcac

30

<210> 86

<211> 10

<212> PRT

<213> artificial sequence

<220>

<223> vH CDR1 VH2,3

<400> 86

Gly Tyr Thr Ala Thr Arg Tyr Thr Met His
1 5 10

<210> 87

<211> 30

<212> DNA

<213> artificial sequence

<220>

<223> vH CDR1 VH5,7

<400> 87
ggctacacct ttactaggta cacgatgcac

30

<210> 88

<211> 10

<212> PRT

<213> artificial sequence

<220>

<223> VH CDR1 VH5,7

<400> 88

Gly Tyr Thr Phe Thr Arg Tyr Thr Met His
1 5 10

<210> 89

<211> 51

<212> DNA

<213> artificial sequence

<220>

<223> VH CDR2 wt anti-CD3 VH7

<400> 89

tacattaatc ctagccgtgg ttataactaat tacaatcaga agttcaagga c

51

<210> 90

<211> 17

<212> PRT

<213> artificial sequence

<220>

<223> VH CDR2 wt anti-CD3 VH7

<400> 90

Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe Lys
1 5 10 15

Asp

<210> 91

<211> 51

<212> DNA

<213> artificial sequence

<220>

<223> VH CDR2 VH5

<400> 91
tacattaatc ctagccgtgg ttataactaat tacgcagaca gcgtcaaggg c

51

<210> 92

<211> 17

<212> PRT

<213> artificial sequence

<220>

<223> VH CDR2 VH5

<400> 92

Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val Lys
1 5 10 15

Gly

<210> 93

<211> 51

<212> DNA

<213> artificial sequence

<220>

<223> VH CDR2 VH2,3

<400> 93
tacattaatc ctagccgtgg ttataactaat tacgcacaga agttgcaggg c

51

<210> 94

<211> 17

<212> PRT

<213> artificial sequence

<220>

<223> VH CDR2 VH2,3

<400> 94

Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Gln Lys Leu Gln
1 5 10 15

Gly

<210> 95

<211> 30

<212> DNA

<213> artificial sequence

<220>

<223> vH CDR3 wt anti-CD3 VH2,3,5,7

<400> 95

tattatgatg atcattactg ccttgactac

30

<210> 96

<211> 10

<212> PRT

<213> artificial sequence

<220>

<223> vH CDR3 wt anti-CD3 VH2,3,5,7

<400> 96

Tyr	Tyr	Asp	Asp	His	Tyr	Cys	Leu	Asp	Tyr
1				5					10

<210> 97

<211> 30

<212> DNA

<213> artificial sequence

<220>

<223> vK CDR1 wt anti-CD3 VL3

<400> 97

agagccagtt caagtgtgtaag ttacatgaac

30

<210> 98

<211> 10

<212> PRT

<213> artificial sequence

<220>

<223> vK CDR1 wt anti-CD3 VL3

<400> 98

Arg Ala Ser Ser Ser Val Ser Tyr Met Asn
 1 5 10

<210> 99

<211> 30

<212> DNA

<213> artificial sequence

<220>

<223> vK CDR1 VL 1,2

<400> 99
 agagccagtc aaagtgtaag ttacatgaac

30

<210> 100

<211> 10

<212> PRT

<213> artificial sequence

<220>

<223> vK CDR1 VL 1,2

<400> 100

Arg Ala Ser Gln Ser Val Ser Tyr Met Asn
 1 5 10

<210> 101

<211> 21

<212> DNA

<213> artificial sequence

<220>

<223> vK CDR2 wt anti-CD3 VL1-3

<400> 101
 gacacatcca aagtggcttc t

21

<210> 102

<211> 7

<212> PRT

<213> artificial sequence

<220>

<223> VK CDR2 wt anti-CD3 VL1-3

<400> 102

Asp Thr Ser Lys Val Ala Ser
1 5

<210> 103

<211> 27

<212> DNA

<213> artificial sequence

<220>

<223> VK CDR3 wt anti-CD3 VL1-3

<400> 103
caacagtgga gtagtaaccc gctcacg

27

<210> 104

<211> 9

<212> PRT

<213> artificial sequence

<220>

<223> VK CDR3 wt anti-CD3 VL1-3

<400> 104

Gln Gln Trp Ser Ser Asn Pro Leu Thr
1 5

<210> 105

<211> 357

<212> DNA

<213> artificial sequence

<220>

<223> VH anti-CD3 with the mutations of cys->ser

<400> 105
 gatatcaaac tgcagcagtc aggggctgaa ctggcaagac ctggggcctc agtgaagatg 60
 tcctgcaaga cttctggcta cacctttact aggtacacga tgcactgggt aaaacagagg 120
 cctggacagg gtctggaatg gattggatac attaatccta gccgtgggta tactaattac 180
 aatcagaagt tcaaggacaa ggccacattg actacagaca aatcctccag cacagcctac 240
 atgcaactga gcagcctgac atctgaggac tctgcagtct attactgtgc aagatattat 300
 gatgatcatt actcccttga ctactggggc caaggcacca ctctcacagt ctcctca 357

<210> 106

<211> 119

<212> PRT

<213> artificial sequence

<220>

<223> vH anti-CD3 with the mutations of cys ->ser

<400> 106

Asp Ile Lys Leu Gln Gln Ser Gly Ala Glu Leu Ala Arg Pro Gly Ala
 1 5 10 15

Ser Val Lys Met Ser Cys Lys Thr Ser Gly Tyr Thr Phe Thr Arg Tyr
 20 25 30

Thr Met His Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile
 35 40 45

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe
 50 55 60

Lys Asp Lys Ala Thr Leu Thr Thr Asp Lys Ser Ser Ser Thr Ala Tyr
 65 70 75 80

Met Gln Leu Ser Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Tyr Cys
 85 90 95

Ala Arg Tyr Tyr Asp Asp His Tyr Ser Leu Asp Tyr Trp Gly Gln Gly
 100 105 110

Thr Thr Leu Thr Val Ser Ser
 115

<210> 107

<211> 30

<212> DNA

<213> artificial sequence

<220>

<223> VH CDR3 anti-CD3 with the mutation cys-> ser

<400> 107

tattatgatg atcattactc ccttgactac

30

<210> 108

<211> 10

<212> PRT

<213> artificial sequence

<220>

<223> VH CDR3 anti-CD3 with the mutation cys-> ser

<400> 108

Tyr Tyr Asp Asp His Tyr Ser Leu Asp Tyr
1 5 10

<210> 109

<211> 357

<212> DNA

<213> artificial sequence

<220>

<223> wild type anti-CD3 VH

<400> 109

gatatcaaac tgcagcagtc aggggctgaa ctggcaagac ctggggcctc agtgaagatg	60
tcctgcaaga cttctggcta cacctttact aggtacacga tgcactgggt aaaacagagg	120
cctggacagg gtctggaatg gattggatac attaatccta gccgtgggta tactaattac	180
aatcagaagt tcaaggacaa ggccacattg actacagaca aatcctccag cacagcctac	240
atgcaactga gcagcctgac atctgaggac tctgcagtct attactgtgc aagatattat	300
gatgatcatt actgccttga ctactggggc caaggcacca ctctcacagt ctcctca	357

<210> 110

<211> 119

<212> PRT

<213> artificial sequence

<220>

<223> wild type anti-CD3 VH

<400> 110

Asp Ile Lys Leu Gln Gln Ser Gly Ala Glu Leu Ala Arg Pro Gly Ala
 1 5 10 15

Ser Val Lys Met Ser Cys Lys Thr Ser Gly Tyr Thr Phe Thr Arg Tyr
 20 25 30

Thr Met His Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile
 35 40 45

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe
 50 55 60

Lys Asp Lys Ala Thr Leu Thr Thr Asp Lys Ser Ser Ser Thr Ala Tyr
 65 70 75 80

Met Gln Leu Ser Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Tyr Cys
 85 90 95

Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
 100 105 110

Thr Thr Leu Thr Val Ser Ser
 115

<210> 111

<211> 318

<212> DNA

<213> artificial sequence

<220>

<223> wild type anti-CD3 VK

<400> 111

gacattcagc tgaccagtc tccagcaatc atgtctgcat ctccagggga gaaggtcacc 60

atgacctgca gagccagttc aagtgttaagt tacatgaact ggtaccagca gaagtcaggc 120

acctcccca aaagatggat ttatgacaca tccaaagtgg cttctggagt cccttatcgc 180

ttcagtggca gtgggtctgg gacctcatac tctctcacia tcagcagcat ggaggctgaa 240

gatgctgcc cttattactg ccaacagtgg agtagtaacc cgctcacgtt cggtgctggg 300

accaagctgg agctgaaa 318

<210> 112

<211> 106

<212> PRT

<213> artificial sequence

<220>

<223> wild type anti-CD3 VK

<400> 112

Asp Ile Gln Leu Thr Gln Ser Pro Ala Ile Met Ser Ala Ser Pro Gly
 1 5 10 15

Glu Lys Val Thr Met Thr Cys Arg Ala Ser Ser Ser Val Ser Tyr Met
 20 25 30

Asn Trp Tyr Gln Gln Lys Ser Gly Thr Ser Pro Lys Arg Trp Ile Tyr
 35 40 45

Asp Thr Ser Lys Val Ala Ser Gly Val Pro Tyr Arg Phe Ser Gly Ser
 50 55 60

Gly Ser Gly Thr Ser Tyr Ser Leu Thr Ile Ser Ser Met Glu Ala Glu
 65 70 75 80

Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr
 85 90 95

Phe Gly Ala Gly Thr Lys Leu Glu Leu Lys
 100 105

<210> 113

<211> 372

<212> DNA

<213> artificial sequence

<220>

<223> CD19 VH

<400> 113

caggtgcagc tgcagcagtc tggggctgag ctggtgagggc ctgggtcctc agtgaagatt	60
tcctgcaagg cttctggcta tgcattcagt agctactgga tgaactgggt gaagcagagg	120
cctggacagg gtcttgagtg gattggacag atttggcctg gagatgggtga tactaactac	180
aatggaaagt tcaagggtaa agccactctg actgcagacg aatcctccag cacagcctac	240
atgcaactca gcagcctagc atctgaggac tctgcggtct atttctgtgc aagacgggag	300
actacgacgg taggccgtta ttactatgct atggactact ggggcccaagg gaccacggtc	360

accgtctcct cc

<210> 114

<211> 124

<212> PRT

<213> artificial sequence

<220>

<223> CD19 VH

<400> 114

Gln val Gln Leu Gln Gln Ser Gly Ala Glu Leu Val Arg Pro Gly Ser
1 5 10 15

Ser val Lys Ile ser Cys Lys Ala Ser Gly Tyr Ala Phe Ser Ser Tyr
20 25 30

Trp Met Asn Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Gln Ile Trp Pro Gly Asp Gly Asp Thr Asn Tyr Asn Gly Lys Phe
50 55 60

Lys Gly Lys Ala Thr Leu Thr Ala Asp Glu Ser Ser Ser Thr Ala Tyr
65 70 75 80

Met Gln Leu Ser Ser Leu Ala Ser Glu Asp Ser Ala Val Tyr Phe Cys
85 90 95

Ala Arg Arg Glu Thr Thr Thr Val Gly Arg Tyr Tyr Tyr Ala Met Asp
100 105 110

Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 115

<211> 333

<212> DNA

<213> artificial sequence

<220>

<223> CD19 VL

<400> 115

gatatccagc tgaccagtc tccagcttct ttggctgtgt ctctagggca gagggccacc 60

atctcctgca aggccagcca aagtgttgat tatgatggtg atagttattt gaactggtac 120

caacagattc caggacagcc acccaaactc ctcatctatg atgcatccaa tctagtttct 180
 gggatccac ccaggtttag tggcagtggg tctgggacag acttcaccct caacatccat 240
 cctgtggaga aggtggatgc tgcaacctat cactgtcagc aaagtactga ggatccgtgg 300
 acgttcggtg gagggaccaa gctcgagatc aaa 333

<210> 116

<211> 111

<212> PRT

<213> artificial sequence

<220>

<223> CD19 VL

<400> 116

Asp Ile Gln Leu Thr Gln Ser Pro Ala Ser Leu Ala Val Ser Leu Gly
 1 5 10 15

Gln Arg Ala Thr Ile Ser Cys Lys Ala Ser Gln Ser Val Asp Tyr Asp
 20 25 30

Gly Asp Ser Tyr Leu Asn Trp Tyr Gln Gln Ile Pro Gly Gln Pro Pro
 35 40 45

Lys Leu Leu Ile Tyr Asp Ala Ser Asn Leu Val Ser Gly Ile Pro Pro
 50 55 60

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Asn Ile His
 65 70 75 80

Pro Val Glu Lys Val Asp Ala Ala Thr Tyr His Cys Gln Gln Ser Thr
 85 90 95

Glu Asp Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
 100 105 110

<210> 117

<211> 47

<212> DNA

<213> artificial sequence

<220>

<223> 4-7 VL BspEI FOR

<400> 117

86
ctgaaatccg gaggtggtgg atccgagctc gtgatgaccc agactcc

47

<210> 118

<211> 52

<212> DNA

<213> artificial sequence

<220>

<223> 4-7 VL GS15 REV

<400> 118
ggagccgccg ccgccagaac caccaccacc tttgatctca agcttggtcc cc

52

<210> 119

<211> 10

<212> PRT

<213> artificial sequence

<220>

<223> CDRH3 M1 mutant

<400> 119

His Tyr Asp Asp His Tyr Cys Leu Asp Tyr
1 5 10

<210> 120

<211> 10

<212> PRT

<213> artificial sequence

<220>

<223> CDRH3 M4 mutant

<400> 120

Tyr Ser Asp Asp His Tyr Cys Leu Asp Tyr
1 5 10

<210> 121

<211> 10

<212> PRT

<213> artificial sequence

<220>

<223> CDRH3 M7 mutant

<400> 121

Tyr Tyr Asp Ala His Tyr Cys Leu Asp Tyr
1 5 10

<210> 122

<211> 10

<212> PRT

<213> artificial sequence

<220>

<223> CDRH3 M9 mutant

<400> 122

Tyr Tyr Asp Asp Gln Tyr Cys Leu Asp Tyr
1 5 10

<210> 123

<211> 10

<212> PRT

<213> artificial sequence

<220>

<223> CDRH3 M10 mutant

<400> 123

Tyr Tyr Asp Asp Pro Tyr Cys Leu Asp Tyr
1 5 10

<210> 124

<211> 10

<212> PRT

<213> artificial sequence

<220>

<223> CDRH3 M11 mutant

<400> 124

Tyr Phe Asn Asp His Tyr Cys Leu Asp Tyr

1 5 10 88

<210> 125
<211> 10
<212> PRT
<213> artificial sequence

<220>

<223> CDRH3 M13 mutant

<400> 125

Tyr Tyr Asn Asp Gln Tyr Cys Leu Asp Tyr
1 5 10

<210> 126
<211> 10
<212> PRT
<213> artificial sequence

<220>

<223> CDRH3 M20 mutant

<400> 126

Tyr His Asp Asp Pro Tyr Cys Leu Asp Tyr
1 5 10

<210> 127
<211> 10
<212> PRT
<213> artificial sequence

<220>

<223> CDRH3 M76 mutant

<400> 127

Tyr Tyr Asp Asp Asn Tyr Cys Leu Asp Tyr
1 5 10

<210> 128
<211> 354
<212> DNA

<213> artificial sequence

<220>

<223> CCR5 Heavy chain

<400> 128

```

cagctggagc agtctggacc tgaactgaag aagcctggag agacagtcac gatctcctgc      60
aaggcttctg ggtatacctt cacgaagttc ggaatgaact gggatgaagca ggctccagga      120
aagggtttaa agtggatggg ctggatacac acctccactg gagagccaac atattctgat      180
gacttcaagg gacggtttgc cttctctttg gaaacgtctg ccagcactgc ctatttgagg      240
atcaacaacc tcaaaaatga ggacatggct aaatacttct gtgccagagg tggtccttac      300
gtaaggggtg ctttggacta ctgggggtcaa ggaacctcag tcaccgtctc ctcc          354

```

<210> 129

<211> 118

<212> PRT

<213> artificial sequence

<220>

<223> CCR5 Heavy chain

<400> 129

```

Gln Leu Glu Gln Ser Gly Pro Glu Leu Lys Lys Pro Gly Glu Thr Val
1           5           10          15

Thr Ile Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Lys Phe Gly Met
          20          25          30

Asn Trp Val Lys Gln Ala Pro Gly Lys Gly Leu Lys Trp Met Gly Trp
          35          40          45

Ile His Thr Ser Thr Gly Glu Pro Thr Tyr Ser Asp Asp Phe Lys Gly
          50          55          60

Arg Phe Ala Phe Ser Leu Glu Thr Ser Ala Ser Thr Ala Tyr Leu Arg
65          70          75          80

Ile Asn Asn Leu Lys Asn Glu Asp Met Ala Lys Tyr Phe Cys Ala Arg
          85          90          95

Gly Gly Pro Tyr Val Arg Gly Ala Leu Asp Tyr Trp Gly Gln Gly Thr
          100         105         110

Ser Val Thr Val Ser Ser
          115

```

<210> 130
 <211> 333
 <212> DNA
 <213> artificial sequence

<220>

<223> CCR5 Light chain

<400> 130
 gacattatcc tgatccaatc tccaccttct ttggctgtgt ctctagggca gagggccacc 60
 atctcctgca gaaccagcga aaatgttgac ggatacggca ttagttttat aaactggtac 120
 caacagaagc caggacagcc acccaaactc ctcattctatg ctgcatccca ccaaggatcc 180
 ggggtccctg ccagatttag tggcagtggg tctgggacag acttcagcct caacatccat 240
 cctttggagg aggatgatac tgcaatgtat ttctgtcacc aaagtaagaa ggttccgtgg 300
 acgttcggtg gaggcaccaa gctggaaatc aaa 333

<210> 131
 <211> 111
 <212> PRT
 <213> artificial sequence

<220>

<223> CCR5 Light chain

<400> 131

Asp Ile Ile Leu Ile Gln Ser Pro Pro Ser Leu Ala Val Ser Leu Gly
 1 5 10 15

Gln Arg Ala Thr Ile Ser Cys Arg Thr Ser Glu Asn Val Asp Gly Tyr
 20 25 30

Gly Ile Ser Phe Ile Asn Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro
 35 40 45

Lys Leu Leu Ile Tyr Ala Ala Ser His Gln Gly Ser Gly Val Pro Ala
 50 55 60

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Ser Leu Asn Ile His
 65 70 75 80

Pro Leu Glu Glu Asp Asp Thr Ala Met Tyr Phe Cys His Gln Ser Lys
 85 90 95

Lys Val Pro Trp Thr Phe Gly Gly Gly Thr⁹¹ Lys Leu Glu Ile Lys
100 105 110

<210> 132

<211> 360

<212> DNA

<213> artificial sequence

<220>

<223> EpCAM5-10 heavy chain

<400> 132

gaggtgcagc tgctcgagca gtctggagct gagctggtaa ggcctgggac ttcagtgaag 60
atattcctgca aggcttctgg atacgccttc actaactact ggctagggttg ggtaaagcag 120
aggcctggac atggacttga gtggattgga gatattttcc ctggaagtgg taatatccac 180
tacaatgaga agttcaaggg caaagccaca ctgactgcag acaaattcttc gagcacagcc 240
tatatgcagc tcagtagcct gacatttgag gactctgctg tctattttctg tgcaagactg 300
aggaactggg acgagcctat ggactactgg ggccaaggga ccacgggtcac cgtctcctca 360

<210> 133

<211> 120

<212> PRT

<213> artificial sequence

<220>

<223> EpCAM5-10 heavy chain

<400> 133

Glu Val Gln Leu⁵ Leu Glu Gln Ser Gly Ala Glu Leu Val Arg Pro Gly
1 10 15
Thr Ser Val Lys²⁰ Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Thr Asn
25 30
Tyr Trp Leu Gly Trp Val Lys Gln Arg Pro Gly His Gly Leu Glu Trp
35 40 45
Ile Gly Asp Ile Phe Pro Gly Ser Gly Asn Ile His Tyr Asn Glu Lys
50 55 60
Phe Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala
65 70 75 80
Tyr Met Gln Leu Ser Ser Leu Thr Phe Glu Asp Ser Ala Val Tyr Phe

85 90 92 95

Cys Ala Arg Leu Arg Asn Trp Asp Glu Pro Met Asp Tyr Trp Gly Gln
100 105 110

Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 134

<211> 339

<212> DNA

<213> artificial sequence

<220>

<223> EpCAM5-10 light chain

<400> 134
gagctcgtga tgacacagtc tccatcctcc ctgactgtga cagcaggaga gaaggctcact 60
atgagctgca agtccagtcga gagtctgtta aacagtggaa atcaaaagaa ctacttgacc 120
tggtaccagc agaaaccagg gcagcctcct aaactgttga tctactgggc atccactagg 180
gaatctgggg tccctgatcg cttcacaggc agtggatctg gaacagattt cactctcacc 240
atcagcagtg tgcaggctga agacctggca gtttattact gtcagaatga ttatagttat 300
ccgctcacgt tcggtgctgg gaccaagctt gagatcaaa 339

<210> 135

<211> 113

<212> PRT

<213> artificial sequence

<220>

<223> EpCAM 5-10 light chain

<400> 135

Glu Leu Val Met Thr Gln Ser Pro Ser Ser Leu Thr Val Thr Ala Gly
1 5 10 15

Glu Lys Val Thr Met Ser Cys Lys Ser Ser Gln Ser Leu Leu Asn Ser
20 25 30

Gly Asn Gln Lys Asn Tyr Leu Thr Trp Tyr Gln Gln Lys Pro Gly Gln
35 40 45

Pro Pro Lys Leu Leu Ile Tyr Trp Ala Ser Thr Arg Glu Ser Gly Val
50 55 60

Pro Asp Arg Phe Thr Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
65 70 75 80

Ile Ser Ser Val Gln Ala Glu Asp Leu Ala Val Tyr Tyr Cys Gln Asn
85 90 95

Asp Tyr Ser Tyr Pro Leu Thr Phe Gly Ala Gly Thr Lys Leu Glu Ile
100 105 110

Lys

<210> 136

<211> 360

<212> DNA

<213> artificial sequence

<220>

<223> EpCAM 3-1 VH

<400> 136

gaggtgcagc tgctcgagca gtctggagct gagctggtga aacctggggc ctcagtgaag	60
atatcctgca aggcttctgg atacgccttc actaactact ggctagggttg ggtaaagcag	120
aggcctggac atggacttga gtggattgga gatcttttcc ctggaagtgg taatactcac	180
tacaatgaga ggttcagggg caaagccaca ctgactgcag acaaatcctc gagcacagcc	240
tttatgcagc tcagtagcct gacatctgag gactctgctg tctatttctg tgcaagattg	300
aggaactggg acgaggctat ggactactgg ggccaaggga ccacgggtcac cgtctcctca	360

<210> 137

<211> 120

<212> PRT

<213> artificial sequence

<220>

<223> EpCAM 3-1 VH

<400> 137

Glu Val Gln Leu Leu Glu Gln Ser Gly Ala Glu Leu Val Lys Pro Gly
1 5 10 15

Ala Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Thr Asn
20 25 30

Tyr Trp Leu Gly Trp Val Lys Gln Arg Pro Gly His Gly Leu Glu Trp
 35 40 45

Ile Gly Asp Leu Phe Pro Gly Ser Gly Asn Thr His Tyr Asn Glu Arg
 50 55 60

Phe Arg Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala
 65 70 75 80

Phe Met Gln Leu Ser Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Phe
 85 90 95

Cys Ala Arg Leu Arg Asn Trp Asp Glu Ala Met Asp Tyr Trp Gly Gln
 100 105 110

Gly Thr Thr Val Thr Val Ser Ser
 115 120

<210> 138

<211> 321

<212> DNA

<213> artificial sequence

<220>

<223> EpCAM 3-1 VL

<400> 138	
gagctcgtca tgaccagtc tccatcttat cttgctgcat ctcctggaga aaccattact	60
attaattgca gggcaagtaa gagcattagc aaatatttag cctgggtatca agagaaacct	120
gggaaaacta ataagcttct tatctactct ggatccactt tgcaatctgg aattccatca	180
aggttcagtg gcagtggatc tggtacagat ttcactctca ccatcagtag cctggagcct	240
gaagattttg caatgtatta ctgtcaacag cataatgaat atccgtacac gttcggaggg	300
gggaccaagc ttgagatcaa a	321

<210> 139

<211> 107

<212> PRT

<213> artificial sequence

<220>

<223> EpCAM 3-1 VL

<400> 139

Glu Leu Val Met Thr Gln Ser Pro Ser Tyr⁹⁵ Leu Ala Ala Ser Pro Gly
 1 5 10 15
 Glu Thr Ile Thr Ile Asn Cys Arg Ala Ser Lys Ser Ile Ser Lys Tyr
 20 25 30
 Leu Ala Trp Tyr Gln Glu Lys Pro Gly Lys Thr Asn Lys Leu Leu Ile
 35 40 45
 Tyr Ser Gly Ser Thr Leu Gln Ser Gly Ile Pro Ser Arg Phe Ser Gly
 50 55 60
 Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Glu Pro
 65 70 75 80
 Glu Asp Phe Ala Met Tyr Tyr Cys Gln Gln His Asn Glu Tyr Pro Tyr
 85 90 95
 Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
 100 105

<210> 140

<211> 372

<212> DNA

<213> artificial sequence

<220>

<223> EpCAM 3-5 VH

<400> 140

gaggtgcagc tgctcgagca gtctggagct gagctggtaa ggcctgggac ttcagtgaag	60
ctgtcctgca aggccttctgg ctacaccttc acaagctatg gtttaagctg ggtgaagcag	120
agaactggac agggccttga gtggattgga gaggtttatc ctagaattgg taatgcttac	180
tacaatgaga agttcaaggg caaggccaca ctgactgcag acaaatcctc cagcacagcg	240
tccatggagc tccgcagcct gacatctgag gactctgcgg tctatttctg tgcaagacgg	300
ggatcctacg gtagtaacta cgactggtac ttcgatgtct ggggcccaagg gaccacggtc	360
accgtctcct ca	372

<210> 141

<211> 124

<212> PRT

<213> artificial sequence

<220>

<223> EpCAM 3-5 VH

<400> 141

Glu Val Gln Leu₅ Leu Glu Gln Ser Gly Ala₁₀ Glu Leu Val Arg Pro Gly₁₅

Thr Ser Val Lys₂₀ Leu Ser Cys Lys Ala₂₅ Ser Gly Tyr Thr Phe₃₀ Thr Ser

Tyr Gly Leu₃₅ Ser Trp Val Lys Gln₄₀ Arg Thr Gly Gln Gly₄₅ Leu Glu Trp

Ile Gly Glu Val Tyr Pro Arg₅₅ Ile Gly Asn Ala Tyr₆₀ Tyr Asn Glu Lys

Phe Lys Gly Lys Ala Thr₇₀ Leu Thr Ala Asp Lys₇₅ Ser Ser Ser Thr Ala₈₀

Ser Met Glu Leu Arg₈₅ Ser Leu Thr Ser Glu₉₀ Asp Ser Ala Val Tyr₉₅ Phe

Cys Ala Arg Arg₁₀₀ Gly Ser Tyr Gly Ser₁₀₅ Asn Tyr Asp Trp Tyr₁₁₀ Phe Asp

Val Trp Gly₁₁₅ Gln Gly Thr Thr Val₁₂₀ Thr Val Ser Ser

<210> 142

<211> 336

<212> DNA

<213> artificial sequence

<220>

<223> EpCAM 3-5 VL

<400> 142	
gagctcgtga tgaccagac tccactctcc ctgcctgtca gtcttgagaga tcaagcctcc	60
atctcttgca gatctagtca gagccttgta cacagtaatg gaaacaccta tttacattgg	120
tacctgcaga agccaggcca gtctccaaag ctctgatct acaaagtttc caaccgattt	180
tctgggggtcc cagacagggt cagtggcagt ggatcaggga cagatttcac actcaagatc	240
agcagagtgg aggctgagga tctgggagtt tatttctgct ctcaaagtac acatgttccg	300
tacacgttcg gaggggggac caagcttgag atcaaa	336

<210> 143

<211> 112

<212> PRT

<213> artificial sequence

<220>

<223> EpCAM 3-5 VL

<400> 143

Glu Leu Val Met Thr Gln Thr Pro Leu Ser Leu Pro Val Ser Leu Gly
1 5 10 15

Asp Gln Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser
20 25 30

Asn Gly Asn Thr Tyr Leu His Trp Tyr Leu Gln Lys Pro Gly Gln Ser
35 40 45

Pro Lys Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Leu Gly Val Tyr Phe Cys Ser Gln Ser
85 90 95

Thr His Val Pro Tyr Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 144

<211> 360

<212> DNA

<213> artificial sequence

<220>

<223> EpCAM 4-1 VH

<400> 144

gaggtgcagc tgctcgagca gtctggagct gagctggtaa ggcctgggac ttcagtgaag	60
atatcctgca aggcttctgg atacgccttc actaactact ggctagggttg ggttaagcag	120
aggcctggac atggacttga atgggttgga gatattttcc ctggaagtgg taatgctcac	180
tacaatgaga agttcaaggg caaagccaca ctgactgcag acaagtcctc gtacacagcc	240
tatatgcagc tcagtagcct gacatctgag gactctgctg tctattttctg tgcaagattg	300
cggaactggg acgaggctat ggactactgg ggccaagggg ccacgggtcac cgtctcctca	360

<210> 145

<211> 120

<212> PRT

<213> artificial sequence

<220>

<223> EpCAM 4-1 VH

<400> 145

Glu Val Gln Leu Leu Glu Gln Ser Gly Ala Glu Leu Val Arg Pro Gly
1 5 10 15

Thr Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Thr Asn
20 25 30

Tyr Trp Leu Gly Trp Val Lys Gln Arg Pro Gly His Gly Leu Glu Trp
35 40 45

Val Gly Asp Ile Phe Pro Gly Ser Gly Asn Ala His Tyr Asn Glu Lys
50 55 60

Phe Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Tyr Thr Ala
65 70 75 80

Tyr Met Gln Leu Ser Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Phe
85 90 95

Cys Ala Arg Leu Arg Asn Trp Asp Glu Ala Met Asp Tyr Trp Gly Gln
100 105 110

Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 146

<211> 339

<212> DNA

<213> artificial sequence

<220>

<223> EpCAM 4-1 VL

<400> 146

gagctcgtga tgacacagtc tccatcctcc ctgagtgtgt cagcaggaga gaaggtcact	60
atgagctgca agtccagtc gagtctgtta aacagtggaa atcaaaagaa ctacttgccc	120
tggtaccagc agaaaccagg gcagcctcct aaactgttga tctacggggc atccactagg	180
gaatctgggg tccctgatcg cttcacaggc agtggatctg gaacagattt cactctcacc	240

atcagcagtg tgcaggctga agacctggca gtttattact gtcagaatga ttatagttat 300
ccgtacacgt tcggagggggg gaccaagctt gagatcaaa 339

<210> 147

<211> 113

<212> PRT

<213> artificial sequence

<220>

<223> EpCAM 4-1 VL

<400> 147

Glu Leu Val Met Thr Gln Ser Pro Ser Ser Leu Ser Val Ser Ala Gly
1 5 10 15

Glu Lys Val Thr Met Ser Cys Lys Ser Ser Gln Ser Leu Leu Asn Ser
20 25 30

Gly Asn Gln Lys Asn Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln
35 40 45

Pro Pro Lys Leu Leu Ile Tyr Gly Ala Ser Thr Arg Glu Ser Gly Val
50 55 60

Pro Asp Arg Phe Thr Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
65 70 75 80

Ile Ser Ser Val Gln Ala Glu Asp Leu Ala Val Tyr Tyr Cys Gln Asn
85 90 95

Asp Tyr Ser Tyr Pro Tyr Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile
100 105 110

Lys

<210> 148

<211> 372

<212> DNA

<213> artificial sequence

<220>

<223> EpCAM 4-7 VH

<400> 148

	100	
gaggtgcagc tgctcgagca gtctggagct gagctggcga ggcctggggc ttcagtgaag		60
ctgtcctgca aggccttctgg ctacaccttc acaaactatg gtttaagctg ggtgaagcag		120
aggcctggac aggtccttga gtggattgga gaggtttatc ctagaattgg taatgcttac		180
tacaatgaga agttcaaggg caaggccaca ctgactgcag acaaatcctc cagcacagcg		240
tccatggagc tccgcagcct gacctctgag gactctgcgg tctattttctg tgcaagacgg		300
ggatcctacg atactaacta cgactgggtac ttcgatgtct ggggccaagg gaccacggtc		360
accgtctcct ca		372

<210> 149

<211> 124

<212> PRT

<213> artificial sequence

<220>

<223> EpCAM 4-7 VH

<400> 149

Glu Val Gln Leu ⁵Leu Glu Gln Ser Gly ¹⁰Ala Glu Leu Ala Arg ¹⁵Pro Gly
1

Ala Ser Val ²⁰Lys Leu Ser Cys Lys ²⁵Ala Ser Gly Tyr Thr ³⁰Phe Thr Asn

Tyr Gly ³⁵Leu Ser Trp Val ⁴⁰Lys Gln Arg Pro Gly Gln ⁴⁵Val Leu Glu Trp

Ile ⁵⁰Gly Glu Val Tyr Pro ⁵⁵Arg Ile Gly Asn Ala ⁶⁰Tyr Tyr Asn Glu Lys

Phe ⁶⁵Lys Gly Lys Ala ⁷⁰Thr Leu Thr Ala Asp ⁷⁵Lys Ser Ser Ser Thr ⁸⁰Ala

Ser Met Glu Leu ⁸⁵Arg Ser Leu Thr Ser ⁹⁰Glu Asp Ser Ala Val ⁹⁵Tyr Phe

Cys Ala Arg ¹⁰⁰Arg Gly Ser Tyr Asp ¹⁰⁵Thr Asn Tyr Asp Trp ¹¹⁰Tyr Phe Asp

Val Trp ¹¹⁵Gly Gln Gly Thr Thr ¹²⁰Val Thr Val Ser Ser

<210> 150

<211> 336

<212> DNA

<213> artificial sequence

<220>

<223> EpCAM 4-7 VL

<400> 150

```

gagctcgtga tgaccagac tccactctcc ctgcctgtca gtcttggaga tcaagcctcc      60
atctcttgca gatctagtca gagccttgta cacagtaatg gaaacaccta ttacattgg      120
tacctgcaga agccaggcca gtctccaaag ctctgatctt acaaagtttc caaccgattt      180
tctgggggtcc cagacagggt cagtggcagt ggatcaggga cagatttcac actcaagatc      240
agcagagtgg aggctgagga tctgggagtt tatttctgct ctcaaagtac acatgttccg      300
tacacgttcg gaggggggac caagcttgag atcaaaa                                336

```

<210> 151

<211> 112

<212> PRT

<213> artificial sequence

<220>

<223> EpCAM 4-7 VL

<400> 151

```

Glu Leu Val Met Thr Gln Thr Pro Leu Ser Leu Pro Val Ser Leu Gly
1          5          10          15
Asp Gln Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser
20        25        30
Asn Gly Asn Thr Tyr Leu His Trp Tyr Leu Gln Lys Pro Gly Gln Ser
35        40        45
Pro Lys Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
50        55        60
Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65        70        75        80
Ser Arg Val Glu Ala Glu Asp Leu Gly Val Tyr Phe Cys Ser Gln Ser
85        90        95
Thr His Val Pro Tyr Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
100       105       110

```

<210> 152

<211> 25

<212> PRT

<213> artificial sequence

<220>

<223> VH5 Framework 1

<400> 152

Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser
20 25

<210> 153

<211> 25

<212> PRT

<213> artificial sequence

<220>

<223> VH7 Framework 1

<400> 153

Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser
20 25

<210> 154

<211> 25

<212> PRT

<213> artificial sequence

<220>

<223> VH2 Framework 1

<400> 154

Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser
20 25

<210> 155
 <211> 25
 <212> PRT
 <213> artificial sequence

<220>

<223> VH3 Framework 1

<400> 155

Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
 1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser
 20 25

<210> 156
 <211> 15
 <212> PRT
 <213> artificial sequence

<220>

<223> VH5 Framework 2

<400> 156

Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr
 1 5 10 15

<210> 157
 <211> 15
 <212> PRT
 <213> artificial sequence

<220>

<223> VH7 Framework 2

<400> 157

Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr
 1 5 10 15

<210> 158
 <211> 22
 <212> PRT

<213> artificial sequence

<220>

<223> VH2 Framework 2

<400> 158

Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile
1 5 10 15

Asn Pro Ser Arg Gly Tyr
20

<210> 159

<211> 22

<212> PRT

<213> artificial sequence

<220>

<223> VH3 Framework 2

<400> 159

Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile
1 5 10 15

Asn Pro Ser Arg Gly Tyr
20

<210> 160

<211> 32

<212> PRT

<213> artificial sequence

<220>

<223> VH5 Framework 3

<400> 160

Arg Phe Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu
1 5 10 15

Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys Ala Arg
20 25 30

<210> 161

<211> 32

<212> PRT

<213> artificial sequence

<220>

<223> VH7 Framework 3

<400> 161

Arg Val Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu
 1 5 10 15

Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg
 20 25 30

<210> 162

<211> 32

<212> PRT

<213> artificial sequence

<220>

<223> VH2 Framework 3

<400> 162

Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr Met Glu
 1 5 10 15

Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys Ala Arg
 20 25 30

<210> 163

<211> 32

<212> PRT

<213> artificial sequence

<220>

<223> VH3 Framework 3

<400> 163

Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr Leu Gln
 1 5 10 15

Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg
 20 25 30

<210> 164
 <211> 11
 <212> PRT
 <213> artificial sequence

<220>
 <223> VH5 Framework 4
 <400> 164
 Trp Gly Gln Gly Thr Thr val Thr val Ser Ser
 1 5 10

<210> 165
 <211> 11
 <212> PRT
 <213> artificial sequence

<220>
 <223> VH7 Framework 4
 <400> 165
 Trp Gly Gln Gly Thr Thr val Thr val Ser Ser
 1 5 10

<210> 166
 <211> 11
 <212> PRT
 <213> artificial sequence

<220>
 <223> VH2 Framework 4
 <400> 166
 Trp Gly Gln Gly Thr Thr val Thr val Ser Ser
 1 5 10

<210> 167
 <211> 11
 <212> PRT
 <213> artificial sequence

<220>

<223> VH3 Framework 4

<400> 167

Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
 1 5 10

<210> 168

<211> 15

<212> PRT

<213> artificial sequence

<220>

<223> standard linker

<400> 168

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
 1 5 10 15

<210> 169

<211> 366

<212> DNA

<213> artificial sequence

<220>

<223> CD20VH

<400> 169

caggtgcaac tgcggcagcc tggggctgag ctggtgaagc ctggggcctc agtgaagatg	60
tcctgcaagg cttctggcta cacatttacc agttacaata tgcactgggt aaagcagaca	120
cctggacagg gcctggaatg gattggagct atttatccag gaaatggtga tacttcctac	180
aatcagaagt tcaaaggcaa ggccacattg actgcagaca aatcctccag cacagcctac	240
atgcagctca gcagtctgac atctgaggac tctgcggtct attactgtgc aagatcgcac	300
tacggtagta actacgtaga ctactttgac tactggggcc aaggcacact agtcacagtc	360
tcgaca	366

<210> 170

<211> 122

<212> PRT

<213> artificial sequence

<220>

<223> CD20VH

<400> 170

Gln Val Gln Leu Arg Gln Pro Gly Ala Glu Leu Val Lys Pro Gly Ala
 1 5 10 15

Ser Val Lys Met Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
 20 25 30

Asn Met His Trp Val Lys Gln Thr Pro Gly Gln Gly Leu Glu Trp Ile
 35 40 45

Gly Ala Ile Tyr Pro Gly Asn Gly Asp Thr Ser Tyr Asn Gln Lys Phe
 50 55 60

Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala Tyr
 65 70 75 80

Met Gln Leu Ser Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Tyr Cys
 85 90 95

Ala Arg Ser His Tyr Gly Ser Asn Tyr Val Asp Tyr Phe Asp Tyr Trp
 100 105 110

Gly Gln Gly Thr Leu Val Thr Val Ser Thr
 115 120

<210> 171

<211> 318

<212> DNA

<213> artificial sequence

<220>

<223> CD20VL

<400> 171
 caaattgttc tctcccagtc tccagcaatc ctttctgcat ctccagggga gaaggtcaca 60
 atgacttgca gggccagctc aagtttaagt ttcatgcact ggtaccagca gaagccagga 120
 tcctcccca aaccctggat ttatgccaca tccaacctgg cttctggagt ccctgctcgc 180
 ttcagtggca gtgggtctgg gacctcttac tctctcacia tcagcagagt ggaggctgaa 240
 gatgctgcca cttatttctg ccatcagtgg agtagtaacc cgctcacgtt cggtgctggg 300
 acaaaggtgg aaataaaa 318

<210> 172
 <211> 106
 <212> PRT
 <213> artificial sequence

<220>

<223> CD20VL

<400> 172

Gln Ile Val Leu Ser Gln Ser Pro Ala Ile Leu Ser Ala Ser Pro Gly
 1 5 10 15

Glu Lys Val Thr Met Thr Cys Arg Ala Ser Ser Ser Leu Ser Phe Met
 20 25 30

His Trp Tyr Gln Gln Lys Pro Gly Ser Ser Pro Lys Pro Trp Ile Tyr
 35 40 45

Ala Thr Ser Asn Leu Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
 50 55 60

Gly Ser Gly Thr Ser Tyr Ser Leu Thr Ile Ser Arg Val Glu Ala Glu
 65 70 75 80

Asp Ala Ala Thr Tyr Phe Cys His Gln Trp Ser Ser Asn Pro Leu Thr
 85 90 95

Phe Gly Ala Gly Thr Lys Val Glu Ile Lys
 100 105

<210> 173

<211> 15

<212> DNA

<213> artificial sequence

<220>

<223> GGGGS linker

<400> 173
 ggaggtggtg gatcc

<210> 174

<211> 5

<212> PRT

<213> artificial sequence

<220>

<223> GGGGS linker

<400> 174

Gly Gly Gly Gly Ser
 1 5

<210> 175

<211> 18

<212> DNA

<213> artificial sequence

<220>

<223> SGGGS linker

<400> 175
 tccggaggtg gtggatcc

18

<210> 176

<211> 6

<212> PRT

<213> artificial sequence

<220>

<223> SGGGS linker

<400> 176

Ser Gly Gly Gly Gly Ser
 1 5

<210> 177

<211> 1527

<212> DNA

<213> artificial sequence

<220>

<223> antiCD19xantiCD3 VH2VL1

<400> 177
 gatatccagc tgaccagtc tccagcttct ttggctgtgt ctctagggca gagggccacc 60
 atctcctgca aggccagcca aagtgttgat tatgatgggtg atagttattt gaactggtac 120

caacagattc caggacagcc acccaaactc ctcatctatg atgcatccaa tctagtttct	180
gggatcccac ccaggtttag tggcagtggg tctgggacag acttcaccct caacatccat	240
cctgtggaga aggtggatgc tgcaacctat cactgtcagc aaagtactga ggatccgtgg	300
acgttcggtg gagggaccaa gctcgagatc aaagggtggtg gtggttcttg cggcggcggc	360
tccggtggtg gtggttctca ggtgcagctg cagcagtctg gggctgagct ggtgaggcct	420
gggtcctcag tgaagatttc ctgcaaggct tctggctatg cattcagtag ctactggatg	480
aactgggtga agcagaggcc tggacagggt cttgagtgga ttggacagat ttggcctgga	540
gatggtgata ctaactacaa tggaaagttc aagggttaaag ccactctgac tgcagacgaa	600
tcctccagca cagcctacat gcaactcagc agcctagcat ctgaggactc tgcggtctat	660
ttctgtgcaa gacgggagac tacgacggta ggccgttatt actatgctat ggactactgg	720
ggccaaggga ccacggtcac cgtctcctcc ggagggtggtg gctccgacgt ccaactggtg	780
cagtcagggg ctgaagtga aaacactggg gcctcagtga aggtgtcctg caaggcttct	840
ggctacaccg ctactaggta cacgatgcac tgggtaaggc aggcacctgg acagggtctg	900
gaatggattg gatacattaa tcctagccgt gggtatacta attacgcaca gaagttgcag	960
ggccgcgtca caatgactac agacacttcc accagcacag cctacatgga actgagcagc	1020
ctgcgttctg aggacactgc aacctattac tgtgcaagat attatgatga tcattactgc	1080
cttgactact ggggccaagg caccacggtc accgtctcct caggcgaagg tactagtact	1140
ggttctggtg gaagtggagg ttcagggtgga gcagacgaca ttcagatgac ccagtctcca	1200
tctagcctgt ctgcatctgt cggggaccgt gtcaccatca cctgcagagc cagtcaaagt	1260
gtaagttaca tgaactggta ccagcagaag ccgggcaagg caccctaaaag atggatttat	1320
gacacatcca aagtggcttc tggagtcctt gctcgcttca gtggcagtgg gtctgggacc	1380
gactactctc tcacaatcaa cagcttggag gctgaagatg ctgccactta ttactgcca	1440
cagtggagta gtaacccgct cacgttcggt ggcgggacca aggtggagat caaacatcat	1500
caccatcatc attagagatc tgtcgac	1527

<210> 178

<211> 498

<212> PRT

<213> artificial sequence

<220>

<223> antiCD19xantiCD3 VH2VL1

<400> 178

Asp	Ile	Gln	Leu	Thr	Gln	Ser	Pro	Ala	Ser	Leu	Ala	Val	Ser	Leu	Gly
1				5					10					15	

Gln Arg Ala Thr Ile Ser Cys Lys Ala Ser Gln Ser Val Asp Tyr Asp
20 25 30

Gly Asp Ser Tyr Leu Asn Trp Tyr Gln Gln Ile Pro Gly Gln Pro Pro
35 40 45

Lys Leu Leu Ile Tyr Asp Ala Ser Asn Leu Val Ser Gly Ile Pro Pro
50 55 60

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Asn Ile His
65 70 75 80

Pro Val Glu Lys Val Asp Ala Ala Thr Tyr His Cys Gln Gln Ser Thr
85 90 95

Glu Asp Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Gly
100 105 110

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Val
115 120 125

Gln Leu Gln Gln Ser Gly Ala Glu Leu Val Arg Pro Gly Ser Ser Val
130 135 140

Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Ser Ser Tyr Trp Met
145 150 155 160

Asn Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile Gly Gln
165 170 175

Ile Trp Pro Gly Asp Gly Asp Thr Asn Tyr Asn Gly Lys Phe Lys Gly
180 185 190

Lys Ala Thr Leu Thr Ala Asp Glu Ser Ser Ser Thr Ala Tyr Met Gln
195 200 205

Leu Ser Ser Leu Ala Ser Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg
210 215 220

Arg Glu Thr Thr Thr Val Gly Arg Tyr Tyr Tyr Ala Met Asp Tyr Trp
225 230 235 240

Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp
245 250 255

Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser
260 265 270

Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Ala Thr Arg Tyr Thr
275 280 285

Met His Trp Val Arg Gln Ala Pro Gly Gln Gly¹¹³ Leu Glu Trp Ile Gly
 290 295 300
 Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Gln Lys Leu Gln
 305 310 315 320
 Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr Met
 325 330 335
 Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys Ala
 340 345 350
 Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr
 355 360 365
 Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly Gly
 370 375 380
 Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Gln Met Thr Gln Ser Pro
 385 390 395 400
 Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg
 405 410 415
 Ala Ser Gln Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro Gly
 420 425 430
 Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser Gly
 435 440 445
 Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser Leu
 450 455 460
 Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys Gln
 465 470 475 480
 Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu
 485 490 495

Ile Lys

<210> 179

<211> 1527

<212> DNA

<213> artificial sequence

<220>

<223> antiCD19xantiCD3 VH2VL2

<400> 179
 gatatccagc tgacccagtc tccagcttct ttggctgtgt ctctagggca gagggccacc 60
 atctcctgca aggccagcca aagtgttgat tatgatggtg atagttattt gaactggtac 120
 caacagattc caggacagcc acccaaactc ctcatctatg atgcatccaa tctagtttct 180
 gggatcccac ccaggtttag tggcagtggg tctgggacag acttcaccct caacatccat 240
 cctgtggaga aggtggatgc tgcaacctat cactgtcagc aaagtactga ggatccgtgg 300
 acgttcggtg gagggacca gctcgagatc aaaggtggtg gtggttctgg cggcggcggc 360
 tccggtggtg gtggttctca ggtgcagctg cagcagtctg gggctgagct ggtgaggcct 420
 gggtcctcag tgaagatttc ctgcaaggct tctggctatg cattcagtag ctactggatg 480
 aactgggtga agcagaggcc tggacagggt cttgagtgga ttggacagat ttggcctgga 540
 gatggtgata ctaactacaa tggaaagtcc aagggtaaag ccactctgac tgcagacgaa 600
 tcctccagca cagcctacat gcaactcagc agcctagcat ctgaggactc tgcggtctat 660
 ttctgtgcaa gacgggagac tacgacggta ggccgttatt actatgctat ggactactgg 720
 ggccaaggga ccacggtcac cgtctcctcc ggaggtggtg gctccgacgt ccaactgggtg 780
 cagtcagggg ctgaagtga aaaacctggg gcctcagtga aggtgtcctg caaggcttct 840
 ggctacaccg ctactaggta cacgatgcac tgggtaaggc aggcacctgg acagggctctg 900
 gaatggattg gatacatcaa tcctagccgt gggtatacta attacgcaca gaagttgcag 960
 ggccgcgtca caatgactac agacacttcc accagcacag cctacatgga actgagcagc 1020
 ctgcggttctg aggacactgc aacctattac tgtgcaagat attatgatga tcattactgc 1080
 cttgactact ggggccaagg caccacggtc accgtctcct caggcgaagg tactagtact 1140
 ggttctggtg gaagtggagg ttcaggtgga gcagacgaca ttgtactgac ccagtctcca 1200
 gcaactctgt ctctgtctcc aggggagcgt gccaccctga gctgcagagc cagtcaaagt 1260
 gtaagttaca tgaactggta ccagcagaag ccgggcaagg cacccaaaag atggatttat 1320
 gacacatcca aagtggcttc tggagtccct gctcgcttca gtggcagtgg gtctgggacc 1380
 gactactctc tcacaatcaa cagcttggag gctgaagatg ctgccactta ttactgcca 1440
 cagtggagta gtaaccgct cacgttcggt ggcgggacca aggtggagat caaacatcat 1500
 caccatcatc attagagatc tgtcgac 1527

<210> 180

<211> 498

<212> PRT

<213> artificial sequence

<220>

<223> antiCD19xantiCD3 VH2VL2

<400> 180

Asp Ile Gln Leu Thr Gln Ser Pro Ala Ser Leu Ala Val Ser Leu Gly
 1 5 10 15

Gln Arg Ala Thr Ile Ser Cys Lys Ala Ser Gln Ser Val Asp Tyr Asp
 20 25 30

Gly Asp Ser Tyr Leu Asn Trp Tyr Gln Gln Ile Pro Gly Gln Pro Pro
 35 40 45

Lys Leu Leu Ile Tyr Asp Ala Ser Asn Leu Val Ser Gly Ile Pro Pro
 50 55 60

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Asn Ile His
 65 70 75 80

Pro Val Glu Lys Val Asp Ala Ala Thr Tyr His Cys Gln Gln Ser Thr
 85 90 95

Glu Asp Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Gly
 100 105 110

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Val
 115 120 125

Gln Leu Gln Gln Ser Gly Ala Glu Leu Val Arg Pro Gly Ser Ser Val
 130 135 140

Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Ser Ser Tyr Trp Met
 145 150 155 160

Asn Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile Gly Gln
 165 170 175

Ile Trp Pro Gly Asp Gly Asp Thr Asn Tyr Asn Gly Lys Phe Lys Gly
 180 185 190

Lys Ala Thr Leu Thr Ala Asp Glu Ser Ser Ser Thr Ala Tyr Met Gln
 195 200 205

Leu Ser Ser Leu Ala Ser Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg
 210 215 220

Arg Glu Thr Thr Thr Val Gly Arg Tyr Tyr Tyr Ala Met Asp Tyr Trp
 225 230 235 240

Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp
 245 250 255

Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser
 260 265 270

Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Ala Thr Arg Tyr Thr
 275 280 285

Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly
 290 295 300

Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Gln Lys Leu Gln
 305 310 315 320

Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr Met
 325 330 335

Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys Ala
 340 345 350

Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr
 355 360 365

Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly Gly
 370 375 380

Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Val Leu Thr Gln Ser Pro
 385 390 395 400

Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg
 405 410 415

Ala Ser Gln Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro Gly
 420 425 430

Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser Gly
 435 440 445

Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser Leu
 450 455 460

Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys Gln
 465 470 475 480

Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu
 485 490 495

Ile Lys

<210> 181

<211> 1527

<212> DNA

<213> artificial sequence

<220>

<223> antiCD19xantiCD3 VH2VL3

<400> 181

gatatccagc	tgacccagtc	tccagcttct	ttggctgtgt	ctctagggca	gagggccacc	60
atctcctgca	aggccagcca	aagtgttgat	tatgatgggtg	atagttattt	gaactgggtac	120
caacagattc	caggacagcc	acccaaaetc	ctcatctatg	atgcatccaa	tctagtttct	180
gggatcccac	ccaggtttag	tggcagtggg	tctgggacag	acttcaccct	caacatccat	240
cctgtggaga	aggtggatgc	tgcaacctat	cactgtcagc	aaagtactga	ggatccgtgg	300
acgttcggtg	gagggacca	gctcgagatc	aaaggtgggtg	gtggttcttg	cggcggcggc	360
tccggtgggtg	gtggtttctca	ggtgcagctg	cagcagtctg	gggctgagct	ggtgaggcct	420
gggtcctcag	tgaagatttc	ctgcaaggct	tctggctatg	cattcagtag	ctactggatg	480
aactgggtga	agcagaggcc	tggacagggt	cttgagtggg	ttggacagat	ttggcctgga	540
gatggtgata	ctaactacaa	tggaaagttc	aagggtaaag	ccactctgac	tgcagacgaa	600
tcctccagca	cagcctacat	gcaactcagc	agcctagcat	ctgaggactc	tgcggtctat	660
ttctgtgcaa	gacgggagac	tacgacggta	ggccgttatt	actatgctat	ggactactgg	720
ggccaaggga	ccacggtcac	cgtctcctcc	ggaggtgggtg	gctccgacgt	ccaactgggtg	780
cagtcagggg	ctgaagtga	aaaacctggg	gcctcagtga	aggtgtcctg	caaggcttct	840
ggctacaccg	ctactaggta	cacgatgcac	tgggtaaggc	aggcacctgg	acaggggtctg	900
gaatggattg	gatacattaa	tcctagccgt	ggttatacta	attacgcaca	gaagttgcag	960
ggccgcgtca	caatgactac	agacacttcc	accagcacag	cctacatgga	actgagcagc	1020
ctgcgttctg	aggacactgc	aacctattac	tgtgcaagat	attatgatga	tcattactgc	1080
cttgactact	ggggccaagg	caccacggtc	accgtctcct	caggcgaagg	tactagtact	1140
ggtttctgggtg	gaagtggagg	ttcaggtgga	gcagacgaca	ttgtactgac	ccagtctcca	1200
gcaactctgt	ctctgtctcc	aggggagcgt	gccaccctga	cctgcagagc	cagttcaagt	1260
gtaagttaca	tgaactggta	ccagcagaag	ccgggcaagg	cacccaaaag	atggatttat	1320
gacacatcca	aagtggcttc	tggagtcctt	gctcgcttca	gtggcagtgg	gtctgggacc	1380
gactactctc	tcacaatcaa	cagcttgag	gctgaagatg	ctgccactta	ttactgccaa	1440
cagtggagta	gtaacccgct	cacgttcggt	ggcgggacca	aggtggagat	caaacatcat	1500
caccatcatc	attagagatc	tgtcgac				1527

<210> 182

<211> 498

<212> PRT

<213> artificial sequence

<220>

<223> antiCD19xantiCD3 VH2VL3

<400> 182

Asp Ile Gln Leu Thr Gln Ser Pro Ala Ser Leu Ala Val Ser Leu Gly
 1 5 10 15

Gln Arg Ala Thr Ile Ser Cys Lys Ala Ser Gln Ser Val Asp Tyr Asp
 20 25 30

Gly Asp Ser Tyr Leu Asn Trp Tyr Gln Gln Ile Pro Gly Gln Pro Pro
 35 40 45

Lys Leu Leu Ile Tyr Asp Ala Ser Asn Leu Val Ser Gly Ile Pro Pro
 50 55 60

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Asn Ile His
 65 70 75 80

Pro Val Glu Lys Val Asp Ala Ala Thr Tyr His Cys Gln Gln Ser Thr
 85 90 95

Glu Asp Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Gly
 100 105 110

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Val
 115 120 125

Gln Leu Gln Gln Ser Gly Ala Glu Leu Val Arg Pro Gly Ser Ser Val
 130 135 140

Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Ser Ser Tyr Trp Met
 145 150 155 160

Asn Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile Gly Gln
 165 170 175

Ile Trp Pro Gly Asp Gly Asp Thr Asn Tyr Asn Gly Lys Phe Lys Gly
 180 185 190

Lys Ala Thr Leu Thr Ala Asp Glu Ser Ser Ser Thr Ala Tyr Met Gln
 195 200 205

Leu Ser Ser Leu Ala Ser Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg
 210 215 220

Arg Glu Thr Thr Thr Val Gly Arg Tyr Tyr Tyr Ala Met Asp Tyr Trp
 225 230 235 240

Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp
 245 250 255

Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser
 260 265 270
 Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Ala Thr Arg Tyr Thr
 275 280 285
 Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly
 290 295 300
 Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Gln Lys Leu Gln
 305 310 315 320
 Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr Met
 325 330 335
 Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys Ala
 340 345 350
 Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr
 355 360 365
 Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly Gly
 370 375 380
 Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Val Leu Thr Gln Ser Pro
 385 390 395 400
 Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Thr Cys Arg
 405 410 415
 Ala Ser Ser Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro Gly
 420 425 430
 Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser Gly
 435 440 445
 Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser Leu
 450 455 460
 Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys Gln
 465 470 475 480
 Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu
 485 490 495
 Ile Lys

<210> 183

<211> 1527

<212> DNA

<213> artificial sequence

<220>

<223> antiCD19xantiCD3. VH3VL1

<400> 183

gatatccagc tgacccagtc tccagcttct ttggctgtgt ctctagggca gagggccacc	60
atctcctgca aggccagcca aagtgttgat tatgatgggtg atagtatttt gaactggtac	120
caacagattc caggacagcc acccaaactc ctcatctatg atgcatccaa tctagtttct	180
gggatcccac ccaggtttag tggcagtggg tctgggacag acttcaccct caacatccat	240
cctgtggaga aggtggatgc tgcaacctat cactgtcagc aaagtactga ggatccgtgg	300
acgttcggtg gagggaccaa gctcgagatc aaagggtgggtg gtggttcttg cggcggcggc	360
tccggtggtg gtggttctca ggtgcagctg cagcagctctg gggctgagct ggtgaggcct	420
gggtcctcag tgaagatttc ctgcaaggct tctggctatg cattcagtag ctactggatg	480
aactgggtga agcagaggcc tggacagggt cttgagtgga ttggacagat ttggcctgga	540
gatggtgata ctaactacaa tggaaagttc aagggtaaag ccactctgac tgcagacgaa	600
tcctccagca cagcctacat gcaactcagc agcctagcat ctgaggactc tgcggtctat	660
ttctgtgcaa gacgggagac tacgacggta ggccgttatt actatgctat ggactactgg	720
ggccaaggga ccacggtcac cgtctcctcc ggagggtgggtg gctccgacgt ccaactgggtg	780
cagtcagggg ctgaagtga aaaacctggg gcctcagtga aggtgtcctg caaggcttct	840
ggctacaccg ctactaggta cacgatgcac tgggtaaggc aggcacctgg acagggtctg	900
gaatggattg gatacatcaa tcctagccgt gggtatacta attacgcaca gaagttgcag	960
ggccgcgtca caatgactac agacacttcc accagcacag cctacctgca aatgaacagc	1020
ctgaaaactg aggacactgc agtctattac tgtgcaagat attatgatga tcattactgc	1080
cttgactact ggggccaagg caccacggtc accgtctcct caggcgaagg tactagtact	1140
ggttctgggtg gaagtggagg ttcagggtgga gcagacgaca ttcagatgac ccagtctcca	1200
tctagcctgt ctgcatctgt cggggaccgt gtcacatca cctgcagagc cagtcaaagt	1260
gtaagttaca tgaactggta ccagcagaag ccgggcaagg cacccaaaag atggatttat	1320
gacacatcca aagtggcttc tggagtcctt gctcgcttca gtggcagtgg gtctgggacc	1380
gactactctc tcacaatcaa cagcttggag gctgaagatg ctgccactta ttactgcca	1440
cagtggagta gtaaccgct cacgttcggt ggcgggacca aggtggagat caaacatcat	1500
caccatcatc attagagatc tgtcgac	1527

<210> 184

<211> 498

<212> PRT

<213> artificial sequence

<220>

<223> antiCD19xantiCD3 VH3VL1

<400> 184

Asp Ile Gln Leu Thr Gln Ser Pro Ala Ser Leu Ala Val Ser Leu Gly
 1 5 10 15

Gln Arg Ala Thr Ile Ser Cys Lys Ala Ser Gln Ser Val Asp Tyr Asp
 20 25 30

Gly Asp Ser Tyr Leu Asn Trp Tyr Gln Gln Ile Pro Gly Gln Pro Pro
 35 40 45

Lys Leu Leu Ile Tyr Asp Ala Ser Asn Leu Val Ser Gly Ile Pro Pro
 50 55 60

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Asn Ile His
 65 70 75 80

Pro Val Glu Lys Val Asp Ala Ala Thr Tyr His Cys Gln Gln Ser Thr
 85 90 95

Glu Asp Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Gly
 100 105 110

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Val
 115 120 125

Gln Leu Gln Gln Ser Gly Ala Glu Leu Val Arg Pro Gly Ser Ser Val
 130 135 140

Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Ser Ser Tyr Trp Met
 145 150 155 160

Asn Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile Gly Gln
 165 170 175

Ile Trp Pro Gly Asp Gly Asp Thr Asn Tyr Asn Gly Lys Phe Lys Gly
 180 185 190

Lys Ala Thr Leu Thr Ala Asp Glu Ser Ser Ser Thr Ala Tyr Met Gln
 195 200 205

Leu Ser Ser Leu Ala Ser Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg
 210 215 220

Arg Glu Thr Thr Thr Val Gly Arg Tyr Tyr Tyr Ala Met Asp Tyr Trp

225		230		122 235		240
Gly	Gln	Gly	Thr	Thr 245	Val	Thr
					Val	Ser
					Ser	250
					Gly	Gly
					Gly	Gly
					Ser	255
					Asp	
Val	Gln	Leu	Val	Gln	Ser	Gly
					Ala	Glu
					260	265
					Val	Lys
					Lys	Pro
					Gly	270
					Ala	Ser
Val	Lys	Val	Ser	Cys	Lys	Ala
					Ser	280
					Gly	Tyr
					Thr	Ala
					Thr	285
					Arg	Tyr
					Thr	
Met	His	Trp	Val	Arg	Gln	Ala
					Pro	Gly
					Gln	Gly
					Leu	Glu
					Trp	Ile
					Gly	
					300	
Tyr	Ile	Asn	Pro	Ser	Arg	Gly
					Tyr	Thr
					Asn	Tyr
					310	315
					Ala	Gln
					Lys	Leu
					Gln	320
Gly	Arg	Val	Thr	Met	Thr	Thr
					Asp	Thr
					Ser	330
					Thr	Ser
					Thr	Ala
					Tyr	335
					Leu	
Gln	Met	Asn	Ser	Leu	Lys	Thr
					Glu	Asp
					340	345
					Thr	Ala
					Val	Tyr
					Tyr	350
					Cys	Ala
Arg	Tyr	Tyr	Asp	Asp	His	Tyr
					Cys	355
					Leu	Asp
					Tyr	Trp
					Gly	360
					Gln	Gly
					Thr	
Thr	Val	Thr	Val	Ser	Ser	Gly
					Glu	370
					Gly	375
					Thr	Ser
					Thr	380
					Gly	Ser
					Gly	Gly
Ser	Gly	Gly	Ser	Gly	Gly	Ala
					Asp	Asp
					Ile	Gln
					Met	385
					Thr	Gln
					Ser	400
Ser	Ser	Leu	Ser	Ala	Ser	Val
					Gly	Asp
					Arg	Val
					Thr	Ile
					Thr	Cys
					Arg	405
Ala	Ser	Gln	Ser	Val	Ser	Tyr
					Met	Asn
					Trp	Tyr
					Gln	Gln
					Lys	Pro
					Gly	420
Lys	Ala	Pro	Lys	Arg	Trp	Ile
					Tyr	Asp
					Thr	Ser
					Lys	Val
					Ala	435
					Ser	Gly
Val	Pro	Ala	Arg	Phe	Ser	Gly
					Ser	Gly
					Ser	Gly
					Thr	Asp
					Tyr	Ser
					Leu	
Thr	Ile	Asn	Ser	Leu	Glu	Ala
					Glu	Asp
					Ala	Ala
					Thr	Tyr
					Tyr	Cys
					Gln	465
Gln	Trp	Ser	Ser	Asn	Pro	Leu
					Thr	Phe
					Gly	Gly
					Gly	Gly
					Thr	Lys
					Val	Glu
					485	490
Ile	Lys					

<210> 185

<211> 1527

<212> DNA

<213> artificial sequence

<220>

<223> antiCD19xantiCD3 VH3VL2

<400> 185

gatatccagc	tgacccagtc	tccagcttct	ttggctgtgt	ctctagggca	gagggccacc	60
atctcctgca	aggccagcca	aagtgttgat	tatgatgggtg	atagttattt	gaactggtac	120
caacagattc	caggacagcc	acccaaactc	ctcatctatg	atgcatccaa	tctagtttct	180
gggatcccac	ccaggttttag	tggcagtggg	tctgggacag	acttcaccct	caacatccat	240
cctgtggaga	aggtggatgc	tgcaacctat	cactgtcagc	aaagtactga	ggatccgtgg	300
acgttcggtg	gagggaccaa	gctcgagatc	aaaggtgggtg	gtggttcttg	cggcggcggc	360
tccggtgggtg	gtggttctca	ggtgcagctg	cagcagtctg	gggctgagct	ggtgaggcct	420
gggtcctcag	tgaagatttc	ctgcaaggct	tctggctatg	cattcagtag	ctactggatg	480
aactgggtga	agcagaggcc	tggacagggt	cttgagtgga	ttggacagat	ttggcctgga	540
gatgggtgata	ctaactacaa	tggaaagtcc	aagggtaaaag	ccactctgac	tgacagacgaa	600
tcctccagca	cagcctacat	gcaactcagc	agcctagcat	ctgaggactc	tgccggtctat	660
ttctgtgcaa	gacgggagac	tacgacggta	ggccggttatt	actatgctat	ggactactgg	720
ggccaagggga	ccacgggtcac	cgtctcctcc	ggaggtgggtg	gctccgacgt	ccaactgggtg	780
cagtcagggg	ctgaagtga	aaaacctggg	gcctcagtga	aggtgtcctg	caaggcttct	840
ggctacaccg	ctactaggta	cacgatgcac	tgggtaaggc	aggcacctgg	acaggggtctg	900
gaatggattg	gatacattaa	tcctagccgt	ggttataacta	attacgcaca	gaagttgcag	960
ggccgcgtca	caatgactac	agacacttcc	accagcacag	cctacctgca	aatgaacagc	1020
ctgaaaactg	aggacactgc	agtctattac	tgtgcaagat	attatgatga	tcattactgc	1080
cttgactact	ggggccaagg	caccacggtc	accgtctcct	caggcgaagg	tactagtact	1140
ggttctgggtg	gaagtggagg	ttcaggtgga	gcagacgaca	ttgtactgac	ccagtctcca	1200
gcaactctgt	ctctgtctcc	aggggagcgt	gccaccctga	gctgcagagc	cagtcaaagt	1260
gtaagttaca	tgaactggta	ccagcagaag	ccgggcaagg	cacccaaaag	atggatttat	1320
gacacatcca	aagtggcttc	tggagtccct	gctcgcttca	gtggcagtgg	gtctgggacc	1380
gactactctc	tcacaatcaa	cagcttggag	gctgaagatg	ctgccactta	ttactgccaa	1440
cagtggagta	gtaacccgct	cacgttcggt	ggcgggacca	aggtggagat	caaacatcat	1500
caccatcatc	attagagatc	tgctcgac				1527

<210> 186

<211> 498

<212> PRT

<213> artificial sequence

<220>

<223> antiCD19xantiCD3 VH3VL2

<400> 186

Asp Ile Gln Leu Thr Gln Ser Pro Ala Ser Leu Ala Val Ser Leu Gly
 1 5 10 15

Gln Arg Ala Thr Ile Ser Cys Lys Ala Ser Gln Ser Val Asp Tyr Asp
 20 25 30

Gly Asp Ser Tyr Leu Asn Trp Tyr Gln Gln Ile Pro Gly Gln Pro Pro
 35 40 45

Lys Leu Leu Ile Tyr Asp Ala Ser Asn Leu Val Ser Gly Ile Pro Pro
 50 55 60

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Asn Ile His
 65 70 75 80

Pro Val Glu Lys Val Asp Ala Ala Thr Tyr His Cys Gln Gln Ser Thr
 85 90 95

Glu Asp Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Gly
 100 105 110

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Val
 115 120 125

Gln Leu Gln Gln Ser Gly Ala Glu Leu Val Arg Pro Gly Ser Ser Val
 130 135 140

Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Ser Ser Tyr Trp Met
 145 150 155 160

Asn Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile Gly Gln
 165 170 175

Ile Trp Pro Gly Asp Gly Asp Thr Asn Tyr Asn Gly Lys Phe Lys Gly
 180 185 190

Lys Ala Thr Leu Thr Ala Asp Glu Ser Ser Ser Thr Ala Tyr Met Gln
 195 200 205

Leu Ser Ser Leu Ala Ser Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg
 210 215 220 125

Arg Glu Thr Thr Thr Val Gly Arg Tyr Tyr Tyr Ala Met Asp Tyr Trp
 225 230 235 240

Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp
 245 250 255

Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser
 260 265 270

Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Ala Thr Arg Tyr Thr
 275 280 285

Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly
 290 295 300

Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Gln Lys Leu Gln
 305 310 315 320

Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr Leu
 325 330 335

Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr Tyr Cys Ala
 340 345 350

Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr
 355 360 365

Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly Gly
 370 375 380

Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Val Leu Thr Gln Ser Pro
 385 390 395 400

Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg
 405 410 415

Ala Ser Gln Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro Gly
 420 425 430

Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser Gly
 435 440 445

Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser Leu
 450 455 460

Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys Gln
 465 470 475 480

Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu

Ile Lys

<210> 187

<211> 1527

<212> DNA

<213> artificial sequence

<220>

<223> antiCD19xantiCD3 VH3VL3

<400> 187

gatatccagc	tgacccagtc	tccagcttct	ttggctgtgt	ctctagggca	gagggccacc	60
atctcctgca	aggccagcca	aagtgttgat	tatgatggtg	atagttatTT	gaactggtac	120
caacagattc	caggacagcc	acccaaactc	ctcatctatg	atgcatccaa	tctagtttct	180
gggatcccac	ccaggtttag	tggcagtggg	tctgggacag	acttcaccct	caacatccat	240
cctgtggaga	aggtggatgc	tgcaacctat	cactgtcagc	aaagtactga	ggatccgtgg	300
acgttcggtg	gagggaccaa	gctcgagatc	aaaggtggtg	gtggttctgg	cggcggcggc	360
tccggtggtg	gtggttctca	ggtgcagctg	cagcagctctg	gggctgagct	ggtgaggcct	420
gggtcctcag	tgaagatttc	ctgcaaggct	tctggctatg	cattcagtag	ctactggatg	480
aactgggtga	agcagaggcc	tggacagggt	cttgagtgga	ttggacagat	ttggcctgga	540
gatggtgata	ctaactacaa	tggaaagttc	aagggtaaag	ccactctgac	tgacagacgaa	600
tcctccagca	cagcctacat	gcaactcagc	agcctagcat	ctgaggactc	tgcggtctat	660
ttctgtgcaa	gacgggagac	tacgacggta	ggccggttatt	actatgctat	ggactactgg	720
ggccaaggga	ccacggtcac	cgtctcctcc	ggaggtggtg	gctccgacgt	ccaactggtg	780
cagtcagggg	ctgaagtga	aaaacctggg	gcctcagtga	aggtgtcctg	caaggcttct	840
ggctacaccg	ctactaggta	cacgatgcac	tgggtaaggc	aggcacctgg	acaggggtctg	900
gaatggattg	gatacattaa	tcctagccgt	ggttatacta	attacgcaca	gaagttgcag	960
ggccgcgtca	caatgactac	agacacttcc	accagcacag	cctacctgca	aatgaacagc	1020
ctgaaaactg	aggacactgc	agtctattac	tgtgcaagat	attatgatga	tcattactgc	1080
cttgactact	ggggccaagg	caccacggtc	accgtctcct	caggcgaagg	tactagtact	1140
ggttctggtg	gaagtggagg	ttcaggtgga	gcagacgaca	ttgtactgac	ccagtctcca	1200
gcaactctgt	ctctgtctcc	aggggagcgt	gccaccctga	cctgcagagc	cagttcaagt	1260
gtaagttaca	tgaactggta	ccagcagaag	ccgggcaagg	cacccaaaag	atggatttat	1320
gacacatcca	aagtggcttc	tggagtccct	gctcgcttca	gtggcagtgg	gtctgggacc	1380
gactactctc	tcacaatcaa	cagcttggag	gctgaagatg	ctgccactta	ttactgccaa	1440

cagtggagta gtaacccgct cacgttcggt ggcgggacca aggtggagat caaacatcat 1500
 caccatcatc attagagatc tgtcgac 1527

<210> 188

<211> 498

<212> PRT

<213> artificial sequence

<220>

<223> antiCD19xantiCD3 VH3VL3

<400> 188

Asp Ile Gln Leu Thr Gln Ser Pro Ala Ser Leu Ala Val Ser Leu Gly
 1 5 10 15

Gln Arg Ala Thr Ile Ser Cys Lys Ala Ser Gln Ser Val Asp Tyr Asp
 20 25 30

Gly Asp Ser Tyr Leu Asn Trp Tyr Gln Gln Ile Pro Gly Gln Pro Pro
 35 40 45

Lys Leu Leu Ile Tyr Asp Ala Ser Asn Leu Val Ser Gly Ile Pro Pro
 50 55 60

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Asn Ile His
 65 70 75 80

Pro Val Glu Lys Val Asp Ala Ala Thr Tyr His Cys Gln Gln Ser Thr
 85 90 95

Glu Asp Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Gly
 100 105 110

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Val
 115 120 125

Gln Leu Gln Gln Ser Gly Ala Glu Leu Val Arg Pro Gly Ser Ser Val
 130 135 140

Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Ser Ser Tyr Trp Met
 145 150 155 160

Asn Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile Gly Gln
 165 170 175

Ile Trp Pro Gly Asp Gly Asp Thr Asn Tyr Asn Gly Lys Phe Lys Gly
 180 185 190

Lys Ala Thr Leu Thr Ala Asp Glu Ser Ser Ser Thr Ala Tyr Met Gln
 195 200 205

Leu Ser Ser Leu Ala Ser Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg
 210 215 220

Arg Glu Thr Thr Thr Val Gly Arg Tyr Tyr Tyr Ala Met Asp Tyr Trp
 225 230 235 240

Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp
 245 250 255

Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser
 260 265 270

Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Ala Thr Arg Tyr Thr
 275 280 285

Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly
 290 295 300

Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Gln Lys Leu Gln
 305 310 315 320

Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr Leu
 325 330 335

Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr Tyr Cys Ala
 340 345 350

Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr
 355 360 365

Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly Gly
 370 375 380

Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Val Leu Thr Gln Ser Pro
 385 390 395 400

Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Thr Cys Arg
 405 410 415

Ala Ser Ser Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro Gly
 420 425 430

Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser Gly
 435 440 445

Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser Leu
 450 455 460

Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala¹²⁹ Thr Tyr Tyr Cys Gln
 465 470 475 480

Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu
 485 490 495

Ile Lys

<210> 189

<211> 1527

<212> DNA

<213> artificial sequence

<220>

<223> antiCD19xantiCD3 VH5VL1

<400> 189

gatatccagc	tgaccagtc	tccagcttct	ttggctgtgt	ctctagggca	gagggccacc	60
atctcctgca	aggccagcca	aagtgttgat	tatgatggtg	atagttat	gaactggtac	120
caacagattc	caggacagcc	acccaaactc	ctcatctatg	atgcatccaa	tctagtttct	180
gggatcccac	ccaggtttag	tggcagtggg	tctgggacag	acttcaccct	caacatccat	240
cctgtggaga	aggtggatgc	tgcaacctat	cactgtcagc	aaagtactga	ggatccgtgg	300
acgttcggtg	gagggaccaa	gctcgagatc	aaagggtggtg	gtggttcttg	cggcggcggc	360
tccggtggtg	gtggttctca	ggtgcagctg	cagcagtctg	gggctgagct	ggtgaggcct	420
gggtcctcag	tgaagatttc	ctgcaaggct	tctggctatg	cattcagtag	ctactggatg	480
aactgggtga	agcagaggcc	tggacagggt	cttgagtgga	ttggacagat	ttggcctgga	540
gatggtgata	ctaactacaa	tggaaagttc	aagggtaaag	ccactctgac	tgcagacgaa	600
tcctccagca	cagcctacat	gcaactcagc	agcctagcat	ctgaggactc	tgcggtctat	660
ttctgtgcaa	gacgggagac	tacgacggta	ggccggttatt	actatgctat	ggactactgg	720
ggccaagggg	ccacgggtcac	cgtctcctcc	ggagggtggtg	gctccgacgt	ccaactggtg	780
cagtcagggg	ctgaagtgaa	aaaacctggg	gcctcagtga	aggtgtcctg	caaggcttct	840
ggctacacct	ttactaggta	cacgatgcac	tgggtaaggc	aggcacctgg	acagggtctg	900
gaatggattg	gatacat	taacattaa	tcctagccgt	ggttatacta	attacgcaga	960
ggccgcttca	caatcactac	agacaaatcc	accagcacag	cctacatgga	actgagcagc	1020
ctgcgttctg	aggacactgc	aacctattac	tgtgcaagat	attatgatga	tcattactgc	1080
cttgactact	ggggccaagg	caccacggtc	accgtctcct	caggcgaagg	tactagtact	1140
ggttctggtg	gaagtggagg	ttcagggtgga	gcagacgaca	ttcagatgac	ccagtctcca	1200
tctagcctgt	ctgcatctgt	cggggaccgt	gtcaccatca	cctgcagagc	cagtcaaagt	1260

130

gtaagttaca tgaactggta ccagcagaag ccgggcaagg cacccaaaag atggatttat	1320
gacacatcca aagtggcttc tggagtcctt gctcgcttca gtggcagtggt gtctgggacc	1380
gactactctc tcacaatcaa cagcttggag gctgaagatg ctgccactta ttactgcca	1440
cagtggagta gtaacccgct cacgttcggt ggcgggacca aggtggagat caaacatcat	1500
caccatcatc attagagatc tgtcgac	1527

<210> 190

<211> 498

<212> PRT

<213> artificial sequence

<220>

<223> antiCD19xantiCD3 VH5VL1

<400> 190

Asp	Ile	Gln	Leu	Thr	Gln	Ser	Pro	Ala	Ser	Leu	Ala	Val	Ser	Leu	Gly
1				5					10					15	

Gln	Arg	Ala	Thr	Ile	Ser	Cys	Lys	Ala	Ser	Gln	Ser	Val	Asp	Tyr	Asp
			20					25					30		

Gly	Asp	Ser	Tyr	Leu	Asn	Trp	Tyr	Gln	Gln	Ile	Pro	Gly	Gln	Pro	Pro
		35					40					45			

Lys	Leu	Leu	Ile	Tyr	Asp	Ala	Ser	Asn	Leu	Val	Ser	Gly	Ile	Pro	Pro
	50					55					60				

Arg	Phe	Ser	Gly	Ser	Gly	Ser	Gly	Thr	Asp	Phe	Thr	Leu	Asn	Ile	His
65					70					75				80	

Pro	Val	Glu	Lys	Val	Asp	Ala	Ala	Thr	Tyr	His	Cys	Gln	Gln	Ser	Thr
				85					90					95	

Glu	Asp	Pro	Trp	Thr	Phe	Gly	Gly	Gly	Thr	Lys	Leu	Glu	Ile	Lys	Gly
			100					105					110		

Gly	Gly	Gly	Ser	Gly	Gly	Gly	Gly	Ser	Gly	Gly	Gly	Gly	Ser	Gln	Val
		115					120					125			

Gln	Leu	Gln	Gln	Ser	Gly	Ala	Glu	Leu	Val	Arg	Pro	Gly	Ser	Ser	Val
	130					135					140				

Lys	Ile	Ser	Cys	Lys	Ala	Ser	Gly	Tyr	Ala	Phe	Ser	Ser	Tyr	Trp	Met
145					150					155					160

Asn	Trp	Val	Lys	Gln	Arg	Pro	Gly	Gln	Gly	Leu	Glu	Trp	Ile	Gly	Gln
				165					170					175	

Ile Trp Pro Gly Asp Gly Asp Thr Asn Tyr Asn Gly Lys Phe Lys Gly
 180 185 190
 Lys Ala Thr Leu Thr Ala Asp Glu Ser Ser Ser Thr Ala Tyr Met Gln
 195 200 205
 Leu Ser Ser Leu Ala Ser Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg
 210 215 220
 Arg Glu Thr Thr Thr Val Gly Arg Tyr Tyr Tyr Ala Met Asp Tyr Trp
 225 230 235 240
 Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp
 245 250 255
 Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser
 260 265 270
 Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr
 275 280 285
 Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly
 290 295 300
 Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val Lys
 305 310 315 320
 Gly Arg Phe Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met
 325 330 335
 Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys Ala
 340 345 350
 Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr
 355 360 365
 Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly Gly
 370 375 380
 Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Gln Met Thr Gln Ser Pro
 385 390 395 400
 Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg
 405 410 415
 Ala Ser Gln Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro Gly
 420 425 430
 Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser Gly
 435 440 445

Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser Leu
 450 455 460

Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys Gln
 465 470 475 480

Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu
 485 490 495

Ile Lys

<210> 191

<211> 1527

<212> DNA

<213> artificial sequence

<220>

<223> antiCD19xantiCD3 VH5VL2

<400> 191

gatatccagc tgacccagtc tccagcttct ttggctgtgt ctctagggca gagggccacc	60
atctcctgca aggccagcca aagtgttgat tatgatggtg atagttatTT gaactggtac	120
caacagattc caggacagcc acccaaactc ctcatctatg atgcatccaa tctagtttct	180
gggatccac ccaggtttag tggcagtggg tctgggacag acttcaccct caacatccat	240
cctgtggaga aggtggatgc tgcaacctat cactgtcagc aaagtactga ggatccgtgg	300
acgttcggtg gagggaccaa gctcgagatc aaagggtggtg gtggttctgg cggcggcggc	360
tccggtggtg gtggttctca ggtgcagctg cagcagtctg gggctgagct ggtgaggcct	420
gggtcctcag tgaagatttc ctgcaaggct tctggctatg cattcagtag ctactggatg	480
aactgggtga agcagaggcc tggacagggt cttgagtgga ttggacagat ttggcctgga	540
gatggtgata ctaactacaa tggaaagtTC aagggtaaag ccactctgac tgcagacgaa	600
tcctccagca cagcctacat gcaactcagc agcctagcat ctgaggactc tgcggtctat	660
ttctgtgcaa gacgggagac tacgacggta ggccgttatt actatgctat ggactactgg	720
ggccaaggga ccacggtcac cgtctcctcc ggagggtggtg gctccgacgt ccaactggtg	780
cagtcagggg ctgaagtga aaaacctggg gcctcagtga aggtgtcctg caaggcttct	840
ggctacacct ttactaggta cacgatgcac tgggtaaggc aggcacctgg acagggtctg	900
gaatggattg gatacattaa tcctagccgt ggttatacta attacgcaga cagcgtcaag	960
ggccgcttca caatcactac agacaaatcc accagcacag cctacatgga actgagcagc	1020
ctgcgttctg aggacactgc aacctattac tgtgcaagat attatgatga tcattactgc	1080
cttgactact ggggccaagg caccacggtc accgtctcct caggcgaagg tactagtact	1140

ggttctggtg gaagtggagg ttcaggtgga gcagacgaca ttgtactgac ccagtctcca 1200
 gcaactctgt ctctgtctcc aggggagcgt gccaccctga gctgcagagc cagtcaaagt 1260
 gtaagttaca tgaactggta ccagcagaag ccgggcaagg caccctaaaag atggatttat 1320
 gacacatcca aagtggcttc tggagtcctt gctcgcttca gtggcagtgg gtctgggacc 1380
 gactactctc tcacaatcaa cagcttggag gctgaagatg ctgccactta ttactgccaa 1440
 cagtggagta gtaacccgct cacgttcggt ggcgggacca aggtggagat caaacatcat 1500
 caccatcatc attagagatc tgtcgac 1527

<210> 192

<211> 498

<212> PRT

<213> artificial sequence

<220>

<223> antiCD19xantiCD3 VH5VL2

<400> 192

Asp Ile Gln Leu Thr Gln Ser Pro Ala Ser Leu Ala Val Ser Leu Gly
 1 5 10 15

Gln Arg Ala Thr Ile Ser Cys Lys Ala Ser Gln Ser Val Asp Tyr Asp
 20 25 30

Gly Asp Ser Tyr Leu Asn Trp Tyr Gln Gln Ile Pro Gly Gln Pro Pro
 35 40 45

Lys Leu Leu Ile Tyr Asp Ala Ser Asn Leu Val Ser Gly Ile Pro Pro
 50 55 60

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Asn Ile His
 65 70 75 80

Pro Val Glu Lys Val Asp Ala Ala Thr Tyr His Cys Gln Gln Ser Thr
 85 90 95

Glu Asp Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Gly
 100 105 110

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Val
 115 120 125

Gln Leu Gln Gln Ser Gly Ala Glu Leu Val Arg Pro Gly Ser Ser Val
 130 135 140

Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Ser Ser Tyr Trp Met

145		150		134 155		160
Asn Trp Val Lys	Gln Arg Pro Gly Gln Gly	Leu Glu Trp Ile Gly	Gln			
	165		170		175	
Ile Trp Pro Gly	Asp Gly Asp Thr Asn Tyr Asn Gly Lys	Phe Lys Gly				
	180		185		190	
Lys Ala Thr	Leu Thr Ala Asp Glu Ser Ser Ser Thr	Ala Tyr Met Gln				
	195		200		205	
Leu Ser Ser	Leu Ala Ser Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg					
	210		215		220	
Arg Glu Thr Thr Thr	Val Gly Arg Tyr Tyr Tyr Ala Met Asp Tyr Trp					
	225		230		235	240
Gly Gln Gly Thr Thr	Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp					
	245		250		255	
Val Gln Leu Val Gln Ser Gly Ala Glu	Val Lys Lys Pro Gly Ala Ser					
	260		265		270	
Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr	Arg Tyr Thr					
	275		280		285	
Met His Trp Val Arg Gln Ala Pro Gly Gln Gly	Leu Glu Trp Ile Gly					
	290		295		300	
Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val Lys						
	305		310		315	320
Gly Arg Phe Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met						
	325		330		335	
Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys Ala						
	340		345		350	
Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr						
	355		360		365	
Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly Gly						
	370		375		380	
Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Val Leu Thr Gln Ser Pro						
	385		390		395	400
Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg						
	405		410		415	
Ala Ser Gln Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro Gly						
	420		425		430	

Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser Gly
 435 440 445

Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser Leu
 450 455 460

Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys Gln
 465 470 475 480

Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu
 485 490 495

Ile Lys

<210> 193

<211> 1527

<212> DNA

<213> artificial sequence

<220>

<223> antiCD19xantiCD3 VH5VL3

<400> 193

gatatccagc tgacccagtc tccagcttct ttggctgtgt ctctagggca gagggccacc	60
atctcctgca aggccagcca aagtgttgat tatgatggtg atagtatttt gaactggtac	120
caacagattc caggacagcc acccaaactc ctcattctatg atgcatccaa tctagtttct	180
gggatccac ccaggtttag tggcagtggg tctgggacag acttcaccct caacatccat	240
cctgtggaga aggtggatgc tgcaacctat cactgtcagc aaagtactga ggatccgtgg	300
acgttcggtg gagggaccaa gctcgagatc aaagggtggtg gtggttctgg cggcggcggc	360
tccggtggtg gtggttctca ggtgcagctg cagcagtctg gggctgagct ggtgaggcct	420
gggtcctcag tgaagatttc ctgcaaggct tctggctatg cattcagtag ctactggatg	480
aactgggtga agcagaggcc tggacagggt cttgagtgga ttggacagat ttggcctgga	540
gatggtgata ctaactacaa tggaaagttc aagggtaaag ccactctgac tgcagacgaa	600
tcctccagca cagcctacat gcaactcagc agcctagcat ctgaggactc tgcggtctat	660
ttctgtgcaa gacgggagac tacgacggtg ggccggttatt actatgctat ggactactgg	720
ggccaaggga ccacggtcac cgtctcctcc ggagggtggtg gctccgacgt ccaactggtg	780
cagtcagggg ctgaagtga aaaacctggg gcctcagtga aggtgtcctg caaggcttct	840
ggctacacct ttactaggta cacgatgcac tgggtaaggc aggcacctgg acagggtctg	900
gaatggattg gatacattaa tcctagccgt gggttatacta attacgcaga cagcgtcaag	960

136

ggccgcttca caatcactac agacaaatcc accagcacag cctacatgga actgagcagc	1020
ctgcgttctg aggacactgc aacctattac tgtgcaagat attatgatga tcattactgc	1080
cttgactact ggggccaagg caccacggtc accgtctcct caggcgaagg tactagtact	1140
ggttctggtg gaagtggagg ttcaggtgga gcagacgaca ttgtactgac ccagtctcca	1200
gcaactctgt ctctgtctcc aggggagcgt gccaccctga cctgcagagc cagttcaagt	1260
gtaagttaca tgaactggtg ccagcagaag ccgggcaagg cacccaaaag atggatttat	1320
gacacatcca aagtggcttc tggagtcctt gctcgcttca gtggcagtgg gtctgggacc	1380
gactactctc tcacaatcaa cagcttggag gctgaagatg ctgccactta ttactgccaa	1440
cagtggagta gtaacccgct cacgttcggt ggcgggacca aggtggagat caaacatcat	1500
caccatcatc attagagatc tgtcgac	1527

<210> 194

<211> 498

<212> PRT

<213> artificial sequence

<220>

<223> antiCD19xantiCD3 VH5VL3

<400> 194

Asp Ile Gln Leu Thr Gln Ser Pro Ala Ser Leu Ala Val Ser Leu Gly
1 5 10 15

Gln Arg Ala Thr Ile Ser Cys Lys Ala Ser Gln Ser Val Asp Tyr Asp
20 25 30

Gly Asp Ser Tyr Leu Asn Trp Tyr Gln Gln Ile Pro Gly Gln Pro Pro
35 40 45

Lys Leu Leu Ile Tyr Asp Ala Ser Asn Leu Val Ser Gly Ile Pro Pro
50 55 60

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Asn Ile His
65 70 75 80

Pro Val Glu Lys Val Asp Ala Ala Thr Tyr His Cys Gln Gln Ser Thr
85 90 95

Glu Asp Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Gly
100 105 110

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Val
115 120 125

Gln Leu Gln Gln Ser Gly Ala Glu Leu Val¹³⁷ Arg Pro Gly Ser Ser Val
 130 135 140
 Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Ser Ser Tyr Trp Met
 145 150 155 160
 Asn Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile Gly Gln
 165 170 175
 Ile Trp Pro Gly Asp Gly Asp Thr Asn Tyr Asn Gly Lys Phe Lys Gly
 180 185 190
 Lys Ala Thr Leu Thr Ala Asp Glu Ser Ser Ser Thr Ala Tyr Met Gln
 195 200 205
 Leu Ser Ser Leu Ala Ser Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg
 210 215 220
 Arg Glu Thr Thr Thr Val Gly Arg Tyr Tyr Tyr Ala Met Asp Tyr Trp
 225 230 235 240
 Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp
 245 250 255
 Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser
 260 265 270
 Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr
 275 280 285
 Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly
 290 295 300
 Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val Lys
 305 310 315 320
 Gly Arg Phe Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met
 325 330 335
 Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys Ala
 340 345 350
 Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr
 355 360 365
 Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly Gly
 370 375 380
 Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Val Leu Thr Gln Ser Pro
 385 390 395 400
 Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Thr Cys Arg

405 410 138 415
 Ala Ser Ser Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro Gly
 420 425 430
 Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser Gly
 435 440 445
 Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser Leu
 450 455 460
 Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys Gln
 465 470 475 480
 Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu
 485 490 495

Ile Lys

<210> 195

<211> 1527

<212> DNA

<213> artificial sequence

<220>

<223> antiCD19xantiCD3 VH7VL1

<400> 195
 gatatccagc tgaccagtc tccagcttct ttggctgtgt ctctagggca gagggccacc 60
 atctcctgca aggccagcca aagtgttgat tatgatgggtg atagttatgt gaactgggtac 120
 caacagattc caggacagcc acccaaactc ctcatctatg atgcatccaa tctagtttct 180
 gggatccac ccaggtttag tggcagtggtg tctgggacag acttcaccct caacatccat 240
 cctgtggaga aggtggatgc tgcaacctat cactgtcagc aaagtactga ggatccgtgg 300
 acgttcggtg gagggaccaa gctcgagatc aaagggtggtg gtggttctgg cggcggcggc 360
 tccggtggtg gtggttctca ggtgcagctg cagcagctctg gggctgagct ggtgaggcct 420
 gggtcctcag tgaagatttc ctgcaaggct tctggctatg cattcagtag ctactggatg 480
 aactgggtga agcagaggcc tggacagggt cttgagtggg ttggacagat ttggcctgga 540
 gatggtgata ctaactacaa tggaaagtgc aagggttaaag ccactctgac tgcagacgaa 600
 tcctccagca cagcctacat gcaactcagc agcctagcat ctgaggactc tgcggtctat 660
 ttctgtgcaa gacgggagac tacgacggta ggccggttatt actatgctat ggactactgg 720
 ggccaaggga ccacgggtcac cgtctcctcc ggagggtggtg gctccgacgt ccaactgggtg 780
 cagtcagggg ctgaagtga aaaacctggg gcctcagtga aggtgtcctg caaggcttct 840

ggctacacct ttactaggtta cacgatgcac tgggtaaggc aggcacctgg acaggggtctg 900
 gaatggattg gatacattaa tcctagccgt gggtatacta attacaaatca gaagttcaag 960
 gaccgcgtca caatcactac agacaaatcc accagcacag cctacatgga actgagcagc 1020
 ctgcgttctg aggacactgc agtctattac tgtgcaagat attatgatga tcattactgc 1080
 cttgactact ggggccaagg caccacggtc accgtctcct caggcgaagg tactagtact 1140
 gggttctgggtg gaagtggagg ttcaggtgga gcagacgaca ttcagatgac ccagtctcca 1200
 tctagcctgt ctgcatctgt cggggaccgt gtcacatca cctgcagagc cagtcaaagt 1260
 gtaagttaca tgaactggta ccagcagaag ccgggcaagg cacccaaaag atggatttat 1320
 gacacatcca aagtggcttc tggagtcctt gctcgcttca gtggcagtggt gtctgggacc 1380
 gactactctc tcacaatcaa cagcttggag gctgaagatg ctgccactta ttactgcca 1440
 cagtggagta gtaacccgct cacgttcggt ggcgggacca aggtggagat caaacatcat 1500
 caccatcatc attagagatc tgtcgac 1527

<210> 196

<211> 498

<212> PRT

<213> artificial sequence

<220>

<223> antiCD19xantiCD3 VH7VL1

<400> 196

Asp Ile Gln Leu Thr Gln Ser Pro Ala Ser Leu Ala Val Ser Leu Gly
1 5 10 15

Gln Arg Ala Thr Ile Ser Cys Lys Ala Ser Gln Ser Val Asp Tyr Asp
20 25 30

Gly Asp Ser Tyr Leu Asn Trp Tyr Gln Gln Ile Pro Gly Gln Pro Pro
35 40 45

Lys Leu Leu Ile Tyr Asp Ala Ser Asn Leu Val Ser Gly Ile Pro Pro
50 55 60

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Asn Ile His
65 70 75 80

Pro Val Glu Lys Val Asp Ala Ala Thr Tyr His Cys Gln Gln Ser Thr
85 90 95

Glu Asp Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Gly
100 105 110

140

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Val
115 120 125

Gln Leu Gln Gln Ser Gly Ala Glu Leu Val Arg Pro Gly Ser Ser Val
130 135 140

Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Ser Ser Tyr Trp Met
145 150 155 160

Asn Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile Gly Gln
165 170 175

Ile Trp Pro Gly Asp Gly Asp Thr Asn Tyr Asn Gly Lys Phe Lys Gly
180 185 190

Lys Ala Thr Leu Thr Ala Asp Glu Ser Ser Ser Thr Ala Tyr Met Gln
195 200 205

Leu Ser Ser Leu Ala Ser Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg
210 215 220

Arg Glu Thr Thr Thr Val Gly Arg Tyr Tyr Tyr Ala Met Asp Tyr Trp
225 230 235 240

Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp
245 250 255

Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser
260 265 270

Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr
275 280 285

Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly
290 295 300

Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe Lys
305 310 315 320

Asp Arg Val Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met
325 330 335

Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala
340 345 350

Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr
355 360 365

Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly Gly
370 375 380

Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile¹⁴¹ Gln Met Thr Gln Ser Pro
385 390 395 400

Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg
405 410 415

Ala Ser Gln Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro Gly
420 425 430

Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser Gly
435 440 445

Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser Leu
450 455 460

Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys Gln
465 470 475 480

Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu
485 490 495

Ile Lys

<210> 197

<211> 1527

<212> DNA

<213> artificial sequence

<220>

<223> antiCD19xantiCD3 VH7VL2

<400> 197

gatatccagc	tgacccagtc	tccagcttct	ttggctgtgt	ctctagggca	gagggccacc	60
atctcctgca	aggccagcca	aagtgttgat	tatgatggtg	atagttat	gaactggtac	120
caacagattc	caggacagcc	acccaaactc	ctcatctatg	atgcatccaa	tctagtttct	180
gggatcccac	ccaggtttag	tggcagtggg	tctgggacag	acttcaccct	caacatccat	240
cctgtggaga	aggtggatgc	tgcaacctat	cactgtcagc	aaagtactga	ggatccgtgg	300
acgttcggtg	gagggaccaa	gctcgagatc	aaaggtggtg	gtggttctgg	cggcggcggc	360
tccggtggtg	gtggttctca	ggtgcagctg	cagcagtctg	gggctgagct	ggtgaggcct	420
gggtcctcag	tgaagatttc	ctgcaaggct	tctggctatg	cattcagtag	ctactggatg	480
aactgggtga	agcagaggcc	tggacagggt	cttgagtgga	ttggacagat	ttggcctgga	540
gatggtgata	ctaactacaa	tggaaagtgc	aagggtaaag	ccactctgac	tgcagacgaa	600
tcctccagca	cagcctacat	gcaactcagc	agcctagcat	ctgaggactc	tgcggtctat	660

142

ttctgtgcaa gacgggagac tacgacggta ggccggttatt actatgctat ggactactgg	720
ggccaagggga ccacggtcac cgtctcctcc ggaggtgggtg gctccgacgt ccaactgggtg	780
cagtcagggg ctgaagtga aaaacctggg gcctcagtga aggtgtcctg caaggcttct	840
ggctacacct ttactaggta cacgatgcac tgggtaaggc aggcacctgg acagggtctg	900
gaatggattg gatacattaa tcctagccgt gggtatacta attacaaatca gaagttcaag	960
gaccgcgtca caatcactac agacaaatcc accagcacag cctacatgga actgagcagc	1020
ctgcgttctg aggacactgc agtctattac tgtgcaagat attatgatga tcattactgc	1080
cttgactact ggggccaagg caccacggtc accgtctcct caggcgaagg tactagtact	1140
ggttctgggtg gaagtggagg ttcagggtgga gcagacgaca ttgtactgac ccagtctcca	1200
gcaactctgt ctctgtctcc aggggagcgt gccaccctga gctgcagagc cagtcaaagt	1260
gtaagttaca tgaactggta ccagcagaag ccgggcaagg cacccaaaag atggatttat	1320
gacacatcca aagtggcttc tggagtcctt gctcgcttca gtggcagtgg gtctgggacc	1380
gactactctc tcacaatcaa cagcttggag gctgaagatg ctgccactta ttactgccaa	1440
cagtggagta gtaacccgct cacgttcggt ggcgggacca aggtggagat caaacatcat	1500
caccatcatc attagagatc tgtcgac	1527

<210> 198

<211> 498

<212> PRT

<213> artificial sequence

<220>

<223> antiCD19xantiCD3 VH7VL2

<400> 198

Asp Ile Gln Leu Thr Gln Ser Pro Ala Ser Leu Ala Val Ser Leu Gly
1 5 10 15

Gln Arg Ala Thr Ile Ser Cys Lys Ala Ser Gln Ser Val Asp Tyr Asp
20 25 30

Gly Asp Ser Tyr Leu Asn Trp Tyr Gln Gln Ile Pro Gly Gln Pro Pro
35 40 45

Lys Leu Leu Ile Tyr Asp Ala Ser Asn Leu Val Ser Gly Ile Pro Pro
50 55 60

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Asn Ile His
65 70 75 80

Pro Val Glu Lys Val Asp Ala Ala Thr Tyr His Cys Gln Gln Ser Thr
85 90 95

Glu Asp Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Gly
 100 105 110
 Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Val
 115 120 125
 Gln Leu Gln Gln Ser Gly Ala Glu Leu Val Arg Pro Gly Ser Ser Val
 130 135 140
 Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Ser Ser Tyr Trp Met
 145 150 155 160
 Asn Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile Gly Gln
 165 170 175
 Ile Trp Pro Gly Asp Gly Asp Thr Asn Tyr Asn Gly Lys Phe Lys Gly
 180 185 190
 Lys Ala Thr Leu Thr Ala Asp Glu Ser Ser Ser Thr Ala Tyr Met Gln
 195 200 205
 Leu Ser Ser Leu Ala Ser Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg
 210 215 220
 Arg Glu Thr Thr Thr Val Gly Arg Tyr Tyr Tyr Ala Met Asp Tyr Trp
 225 230 235 240
 Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp
 245 250 255
 Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser
 260 265 270
 Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr
 275 280 285
 Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly
 290 295 300
 Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe Lys
 305 310 315 320
 Asp Arg Val Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met
 325 330 335
 Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala
 340 345 350
 Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr
 355 360 365

Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly Gly
370 375 380

Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Val Leu Thr Gln Ser Pro
385 390 395 400

Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg
405 410 415

Ala Ser Gln Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro Gly
420 425 430

Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser Gly
435 440 445

Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser Leu
450 455 460

Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys Gln
465 470 475 480

Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu
485 490 495

Ile Lys

<210> 199

<211> 1527

<212> DNA

<213> artificial sequence

<220>

<223> antiCD19xantiCD3 VH7VL3

<400> 199	
gatatccagc tgaccagtc tccagcttct ttggctgtgt ctctagggca gagggccacc	60
atctcctgca aggccagcca aagtgttgat tatgatgggtg atagttattt gaactgggtac	120
caacagattc caggacagcc acccaaactc ctcatctatg atgcatccaa tctagtttct	180
gggatccac ccaggtttag tggcagtggg tctgggacag acttcaccct caacatccat	240
cctgtggaga aggtggatgc tgcaacctat cactgtcagc aaagtactga ggatccgtgg	300
acgttcggtg gagggaccaa gctcgagatc aaagggtggtg gtggttcttg cggcggcggc	360
tccggtgggtg gtggttctca ggtgcagctg cagcagtctg gggctgagct ggtgaggcct	420
gggtcctcag tgaagatttc ctgcaaggct tctggctatg cattcagtag ctactggatg	480
aactgggtga agcagaggcc tggacagggt cttgagtgga ttggacagat ttggcctgga	540

gatggtgata ctaactacaa tggaaagttc aagggttaaag ccactctgac tgcagacgaa 600
 tcctccagca cagcctacat gcaactcagc agcctagcat ctgaggactc tgcggtctat 660
 ttctgtgcaa gacgggagac tacgacggta ggccggttatt actatgctat ggactactgg 720
 ggccaaggga ccacgggtcac cgtctcctcc ggagggtggtg gctccgacgt ccaactggtg 780
 cagtcagggg ctgaagtga aaaacctggg gcctcagtga aggtgtcctg caaggcttct 840
 ggctacacct ttactaggta cacgatgcac tgggtaaggc aggcacctgg acagggtctg 900
 gaatggattg gatacattaa tcctagccgt gggtataacta attacaatca gaagttcaag 960
 gaccgcgtca caatcactac agacaaatcc accagcacag cctacatgga actgagcagc 1020
 ctgcgttctg aggacactgc agtctattac tgtgcaagat attatgatga tcattactgc 1080
 cttgactact ggggccaagg caccacggtc accgtctcct caggcgaagg tactagtact 1140
 gggttctggtg gaagtggagg ttcagggtgga gcagacgaca ttgtactgac ccagtctcca 1200
 gcaactctgt ctctgtctcc aggggagcgt gccaccctga cctgcagagc cagttcaagt 1260
 gtaagttaca tgaactggta ccagcagaag ccgggcaagg cacccaaaag atggatttat 1320
 gacacatcca aagtggcttc tggagtcctt gctcgcttca gtggcagtgg gtctgggacc 1380
 gactactctc tcacaatcaa cagcttgag gctgaagatg ctgccactta ttactgcca 1440
 cagtggagta gtaacccgct cacgttcggt ggcgggacca aggtggagat caaacatcat 1500
 caccatcatc attagagatc tgtcgac 1527

<210> 200

<211> 498

<212> PRT

<213> artificial sequence

<220>

<223> antiCD19xantiCD3 VH7VL3

<400> 200

Asp Ile Gln Leu Thr Gln Ser Pro Ala Ser Leu Ala Val Ser Leu Gly
 1 5 10 15

Gln Arg Ala Thr Ile Ser Cys Lys Ala Ser Gln Ser Val Asp Tyr Asp
 20 25 30

Gly Asp Ser Tyr Leu Asn Trp Tyr Gln Gln Ile Pro Gly Gln Pro Pro
 35 40 45

Lys Leu Leu Ile Tyr Asp Ala Ser Asn Leu Val Ser Gly Ile Pro Pro
 50 55 60

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Asn Ile His

65		70		146 75		80									
Pro	Val	Glu	Lys	Val ₈₅	Asp	Ala	Ala	Thr	Tyr ₉₀	His	Cys	Gln	Gln	Ser ₉₅	Thr
Glu	Asp	Pro	Trp ₁₀₀	Thr	Phe	Gly	Gly	Gly ₁₀₅	Thr	Lys	Leu	Glu	Ile ₁₁₀	Lys	Gly
Gly	Gly	Gly ₁₁₅	Ser	Gly	Gly	Gly	Gly ₁₂₀	Ser	Gly	Gly	Gly	Gly ₁₂₅	Ser	Gln	Val
Gln	Leu ₁₃₀	Gln	Gln	Ser	Gly	Ala ₁₃₅	Glu	Leu	Val	Arg	Pro ₁₄₀	Gly	Ser	Ser	Val
Lys ₁₄₅	Ile	Ser	Cys	Lys	Ala ₁₅₀	Ser	Gly	Tyr	Ala	Phe ₁₅₅	Ser	Ser	Tyr	Trp	Met ₁₆₀
Asn	Trp	Val	Lys	Gln ₁₆₅	Arg	Pro	Gly	Gln	Gly ₁₇₀	Leu	Glu	Trp	Ile	Gly ₁₇₅	Gln
Ile	Trp	Pro	Gly ₁₈₀	Asp	Gly	Asp	Thr	Asn ₁₈₅	Tyr	Asn	Gly	Lys	Phe ₁₉₀	Lys	Gly
Lys	Ala	Thr ₁₉₅	Leu	Thr	Ala	Asp	Glu ₂₀₀	Ser	Ser	Ser	Thr	Ala ₂₀₅	Tyr	Met	Gln
Leu	Ser ₂₁₀	Ser	Leu	Ala	Ser	Glu ₂₁₅	Asp	Ser	Ala	Val	Tyr ₂₂₀	Phe	Cys	Ala	Arg
Arg ₂₂₅	Glu	Thr	Thr	Thr	Val ₂₃₀	Gly	Arg	Tyr	Tyr	Tyr ₂₃₅	Ala	Met	Asp	Tyr	Trp ₂₄₀
Gly	Gln	Gly	Thr	Thr ₂₄₅	Val	Thr	Val	Ser	Ser ₂₅₀	Gly	Gly	Gly	Gly	Ser ₂₅₅	Asp
Val	Gln	Leu	Val ₂₆₀	Gln	Ser	Gly	Ala	Glu ₂₆₅	Val	Lys	Lys	Pro	Gly ₂₇₀	Ala	Ser
Val	Lys	Val ₂₇₅	Ser	Cys	Lys	Ala	Ser ₂₈₀	Gly	Tyr	Thr	Phe	Thr ₂₈₅	Arg	Tyr	Thr

Met ₂₉₀	His	Trp	Val	Arg	Gln	Ala ₂₉₅	Pro	Gly	Gln	Gly	Leu ₃₀₀	Glu	Trp	Ile	Gly
Tyr ₃₀₅	Ile	Asn	Pro	Ser	Arg ₃₁₀	Gly	Tyr	Thr	Asn	Tyr ₃₁₅	Asn	Gln	Lys	Phe	Lys ₃₂₀
Asp	Arg	Val	Thr	Ile ₃₂₅	Thr	Thr	Asp	Lys	Ser ₃₃₀	Thr	Ser	Thr	Ala	Tyr	Met ₃₃₅
Glu	Leu	Ser	Ser ₃₄₀	Leu	Arg	Ser	Glu	Asp ₃₄₅	Thr	Ala	Val	Tyr	Tyr ₃₅₀	Cys	Ala

Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr
 355 360 365

Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly Gly
 370 375 380

Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Val Leu Thr Gln Ser Pro
 385 390 395 400

Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Thr Cys Arg
 405 410 415

Ala Ser Ser Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro Gly
 420 425 430

Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser Gly
 435 440 445

Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser Leu
 450 455 460

Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys Gln
 465 470 475 480

Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu
 485 490 495

Ile Lys

<210> 201

<211> 45

<212> DNA

<213> artificial sequence

<220>

<223> standard linker

<400> 201

ggtggtggtg gttctggcgg cggcggctcc ggtggtggtg gttct

45

<210> 202

<211> 54

<212> DNA

<213> artificial sequence

<220>

<223> deimmunized linker

<400> 202

ggcgaaggta ctagtactgg ttctggtgga agtggagggt caggtggagc agac

54

<210> 203

<211> 1494

<212> DNA

<213> artificial sequence

<220>

<223> antiCD19xantiCD3

<400> 203

gatatccagc tgacccagtc tccagcttct ttggctgtgt ctctagggca gagggccacc	60
atctcctgca aggccagcca aagtgttgat tatgatggtg atagttattt gaactggtac	120
caacagattc caggacagcc acccaaactc ctcatctatg atgcatcaa tctagtttct	180
gggatcccac ccaggtttag tggcagtggg tctgggacag acttcaccct caacatccat	240
cctgtggaga aggtggatgc tgcaacctat cactgtcagc aaagtactga ggatccgtgg	300
acgttcggtg gagggaccaa gctcgagatc aaagggtggtg gtggttcttg cggcggcggc	360
tccggtggtg gtggttctca ggtgcagctg cagcagtctg gggctgagct ggtgaggcct	420
gggtcctcag tgaagatttc ctgcaaggct tctggctatg cattcagtag ctactggatg	480
aactgggtga agcagaggcc tggacagggt cttgagtgga ttggacagat ttggcctgga	540
gatggtgata ctaactacaa tggaaagttc aagggtaaag ccactctgac tgcagacgaa	600
tcctccagca cagcctacat gcaactcagc agcctagcat ctgaggactc tgcggtctat	660
ttctgtgcaa gacgggagac tacgacggta ggccgttatt actatgctat ggactactgg	720
ggccaaggga ccacggtcac cgtctcctcc ggagggtggtg gatccgatat caaactgcag	780
cagtcagggg ctgaactggc aagacctggg gcctcagtga agatgtcctg caagacttct	840
ggctacacct ttactaggta cacgatgcac tgggtaaaac agaggcctgg acagggtctg	900
gaatggattg gatacattaa tcctagccgt ggttatacta attacaatca gaagttcaag	960
gacaaggcca cattgactac agacaaatcc tccagcacag cctacatgca actgagcagc	1020
ctgacatctg aggactctgc agtctattac tgtgcaagat attatgatga tcattactgc	1080
cttgactact ggggccaagg caccactctc acagtctcct cagtcgaagg tggaagtgga	1140
ggttctggtg gaagtggagg ttcagggtgga gtcgacgaca ttcagctgac ccagtctcca	1200
gcaatcatgt ctgcatctcc aggggagaag gtcaccatga cctgcagagc cagttcaagt	1260
gtaagttaca tgaactggta ccagcagaag tcaggcacct ccccaaaaag atggatttat	1320
gacacatcca aagtggcttc tggagtcctt tatcgcttca gtggcagtgg gtctgggacc	1380

tcataactctc tcacaatcag cagcatggag gctgaagatg ctgccactta ttactgccaa 1440
 cagtggagta gtaacccgct cacgttcggt gctgggacca agctggagct gaaa 1494

<210> 204

<211> 498

<212> PRT

<213> artificial sequence

<220>

<223> antiCD19xantiCD3

<400> 204

Asp Ile Gln Leu Thr Gln Ser Pro Ala Ser Leu Ala Val Ser Leu Gly
 1 5 10 15

Gln Arg Ala Thr Ile Ser Cys Lys Ala Ser Gln Ser Val Asp Tyr Asp
 20 25 30

Gly Asp Ser Tyr Leu Asn Trp Tyr Gln Gln Ile Pro Gly Gln Pro Pro
 35 40 45

Lys Leu Leu Ile Tyr Asp Ala Ser Asn Leu Val Ser Gly Ile Pro Pro
 50 55 60

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Asn Ile His
 65 70 75 80

Pro Val Glu Lys Val Asp Ala Ala Thr Tyr His Cys Gln Gln Ser Thr
 85 90 95

Glu Asp Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Gly
 100 105 110

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Val
 115 120 125

Gln Leu Gln Gln Ser Gly Ala Glu Leu Val Arg Pro Gly Ser Ser Val
 130 135 140

Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Ser Ser Tyr Trp Met
 145 150 155 160

Asn Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile Gly Gln
 165 170 175

Ile Trp Pro Gly Asp Gly Asp Thr Asn Tyr Asn Gly Lys Phe Lys Gly
 180 185 190

Lys Ala Thr Leu Thr Ala Asp Glu Ser Ser Ser Thr Ala Tyr Met Gln
195 200 205

Leu Ser Ser Leu Ala Ser Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg
210 215 220

Arg Glu Thr Thr Thr Val Gly Arg Tyr Tyr Tyr Ala Met Asp Tyr Trp
225 230 235 240

Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp
245 250 255

Ile Lys Leu Gln Gln Ser Gly Ala Glu Leu Ala Arg Pro Gly Ala Ser
260 265 270

Val Lys Met Ser Cys Lys Thr Ser Gly Tyr Thr Phe Thr Arg Tyr Thr
275 280 285

Met His Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile Gly
290 295 300

Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe Lys
305 310 315 320

Asp Lys Ala Thr Leu Thr Thr Asp Lys Ser Ser Ser Thr Ala Tyr Met
325 330 335

Gln Leu Ser Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Tyr Cys Ala
340 345 350

Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr
355 360 365

Thr Leu Thr Val Ser Ser Val Glu Gly Gly Ser Gly Gly Ser Gly Gly
370 375 380

Ser Gly Gly Ser Gly Gly Val Asp Asp Ile Gln Leu Thr Gln Ser Pro
385 390 395 400

Ala Ile Met Ser Ala Ser Pro Gly Glu Lys Val Thr Met Thr Cys Arg
405 410 415

Ala Ser Ser Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Ser Gly
420 425 430

Thr Ser Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser Gly
435 440 445

Val Pro Tyr Arg Phe Ser Gly Ser Gly Ser Gly Thr Ser Tyr Ser Leu
450 455 460

Thr Ile Ser Ser Met Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys Gln
 465 470 475 480

Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Ala Gly Thr Lys Leu Glu
 485 490 495

Leu Lys

<210> 205

<211> 1476

<212> DNA

<213> artificial sequence

<220>

<223> CCR5xanti-CD3 VH5VL1

<400> 205

gacattatcc	tgatccaatc	tccaccttct	ttggctgtgt	ctctagggca	gagggccacc	60
atctcctgca	gaaccagcga	aatgttgac	ggatacggca	ttagttttat	aaactggtac	120
caacagaagc	caggacagcc	acccaaactc	ctcatctatg	ctgcatccca	ccaaggatcc	180
ggggtccctg	ccagatttag	tggcagtggg	tctgggacag	acttcagcct	caacatccat	240
cctttggagg	aggatgatac	tgcaatgtat	ttctgtcacc	aaagtaagaa	ggttccgtgg	300
acgttcggtg	gaggcaccaa	gctggaaatc	aaaggtggtg	gtggttcttg	cggcggcggc	360
tccggtggtg	gtggttctca	gctggagcag	tctggacctg	aactgaagaa	gcctggagag	420
acagtcacga	tctcctgcaa	ggcttctggg	tataccttca	cgaagttcgg	aatgaactgg	480
gtgaagcagg	ctccaggaaa	gggttttaaag	tggatgggct	ggatacacac	ctccactgga	540
gagccaacat	attctgatga	cttcaaggga	cggtttgcct	tctctttgga	aacgtctgcc	600
agcactgcct	atttgcggat	caacaacctc	aaaaatgagg	acatggctaa	atacttctgt	660
gccagagggtg	gtccttacgt	aaggggtgct	ttggactact	gggggtcaagg	aacctcagtc	720
accgtctcct	ccggagggtg	tggatccgac	gtccaactgg	tgcagtcagg	ggctgaagtg	780
aaaaaacctg	gggcctcagt	gaagggtgtc	tgcaaggctt	ctggctacac	ctttactagg	840
tacacgatgc	actgggtaag	gcaggcacct	ggacagggtc	tggaatggat	tggatacatt	900
aatcctagcc	gtggttatac	taattacgca	gacagcgtca	agggccgctt	cacaatcact	960
acagacaaat	ccaccagcac	agcctacatg	gaactgagca	gcctgcgttc	tgaggacact	1020
gcaacctatt	actgtgcaag	atattatgat	gatcattact	gccttgacta	ctggggccaa	1080
ggcaccacgg	tcaccgtctc	ctcaggcgaa	ggtagtagta	ctggttcttg	tggaagtgga	1140
ggttcagggtg	gagcagacga	cattcagatg	accagtcctc	catctagcct	gtctgcatct	1200
gtcggggacc	gtgtcaccat	cacctgcaga	gccagtcaaa	gtgtaagtta	catgaactgg	1260

152

taccagcaga agccgggcaa ggcacccaaa agatggattt atgacacatc caaagtggct	1320
tctggagtcc ctgctcgctt cagtggcagt gggctctggga ccgactactc tctcacaatc	1380
aacagcttgg aggctgaaga tgctgccact tattactgcc aacagtggag tagtaacccg	1440
ctcacgttcg gtggcgggac caaggtggag atcaaa	1476

<210> 206
 <211> 492
 <212> PRT
 <213> artificial sequence

<220>
 <223> CCR5xanti-CD3 VH5VL1
 <400> 206

Asp Ile Ile Leu Ile Gln Ser Pro Pro Ser Leu Ala Val Ser Leu Gly
 1 5 10 15

Gln Arg Ala Thr Ile Ser Cys Arg Thr Ser Glu Asn Val Asp Gly Tyr
 20 25 30

Gly Ile Ser Phe Ile Asn Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro
 35 40 45

Lys Leu Leu Ile Tyr Ala Ala Ser His Gln Gly Ser Gly Val Pro Ala
 50 55 60

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Ser Leu Asn Ile His
 65 70 75 80

Pro Leu Glu Glu Asp Asp Thr Ala Met Tyr Phe Cys His Gln Ser Lys
 85 90 95

Lys Val Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Gly
 100 105 110

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Leu
 115 120 125

Glu Gln Ser Gly Pro Glu Leu Lys Lys Pro Gly Glu Thr Val Thr Ile
 130 135 140

Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Lys Phe Gly Met Asn Trp
 145 150 155 160

Val Lys Gln Ala Pro Gly Lys Gly Leu Lys Trp Met Gly Trp Ile His
 165 170 175

Thr Ser Thr Gly Glu Pro Thr Tyr Ser Asp Asp¹⁵³ Phe Lys Gly Arg Phe
 180 185 190

Ala Phe Ser Leu Glu Thr Ser Ala Ser Thr Ala Tyr Leu Arg Ile Asn
 195 200 205

Asn Leu Lys Asn Glu Asp Met Ala Lys Tyr Phe Cys Ala Arg Gly Gly
 210 215 220

Pro Tyr Val Arg Gly Ala Leu Asp Tyr Trp Gly Gln Gly Thr Ser Val
 225 230 235 240

Thr Val Ser Ser Gly Gly Gly Gly Ser Asp Val Gln Leu Val Gln Ser
 245 250 255

Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys
 260 265 270

Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp Val Arg Gln
 275 280 285

Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn Pro Ser Arg
 290 295 300

Gly Tyr Thr Asn Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Thr
 305 310 315 320

Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg
 325 330 335

Ser Glu Asp Thr Ala Thr Tyr Tyr Cys Ala Arg Tyr Tyr Asp Asp His
 340 345 350

Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
 355 360 365

Gly Glu Gly Thr Ser Thr Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly
 370 375 380

Ala Asp Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser
 385 390 395 400

Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Ser
 405 410 415

Tyr Met Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp
 420 425 430

Ile Tyr Asp Thr Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser
 435 440 445

Gly Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu

tctggagtcc ctgctcgctt cagtggcagt gggctctggga ccgactactc tctcacaatc 1380
 aacagcttgg aggctgaaga tgctgccact tattactgcc aacagtggag tagtaaccgc 1440
 ctcacgttcg gtggcgggac caaggtggag atcaaaa 1476

<210> 208

<211> 492

<212> PRT

<213> artificial sequence

<220>

<223> CCR5xanti-CD3 VH5VL2

<400> 208

Asp Ile Ile Leu Ile Gln Ser Pro Pro Ser Leu Ala Val Ser Leu Gly
 1 5 10 15

Gln Arg Ala Thr Ile Ser Cys Arg Thr Ser Glu Asn Val Asp Gly Tyr
 20 25 30

Gly Ile Ser Phe Ile Asn Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro
 35 40 45

Lys Leu Leu Ile Tyr Ala Ala Ser His Gln Gly Ser Gly Val Pro Ala
 50 55 60

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Ser Leu Asn Ile His
 65 70 75 80

Pro Leu Glu Glu Asp Asp Thr Ala Met Tyr Phe Cys His Gln Ser Lys
 85 90 95

Lys Val Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Gly
 100 105 110

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Leu
 115 120 125

Glu Gln Ser Gly Pro Glu Leu Lys Lys Pro Gly Glu Thr Val Thr Ile
 130 135 140

Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Lys Phe Gly Met Asn Trp
 145 150 155 160

Val Lys Gln Ala Pro Gly Lys Gly Leu Lys Trp Met Gly Trp Ile His
 165 170 175

Thr Ser Thr Gly Glu Pro Thr Tyr Ser Asp Asp Phe Lys Gly Arg Phe

180 185 156 190
 Ala Phe Ser Leu Glu Thr Ser Ala Ser Thr Ala Tyr Leu Arg Ile Asn
 195 200 205
 Asn Leu Lys Asn Glu Asp Met Ala Lys Tyr Phe Cys Ala Arg Gly Gly
 210 215 220
 Pro Tyr Val Arg Gly Ala Leu Asp Tyr Trp Gly Gln Gly Thr Ser Val
 225 230 235 240
 Thr Val Ser Ser Gly Gly Gly Gly Ser Asp Val Gln Leu Val Gln Ser
 245 250 255
 Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys
 260 265 270
 Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp Val Arg Gln
 275 280 285
 Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn Pro Ser Arg
 290 295 300
 Gly Tyr Thr Asn Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Thr
 305 310 315 320
 Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg
 325 330 335
 Ser Glu Asp Thr Ala Thr Tyr Tyr Cys Ala Arg Tyr Tyr Asp Asp His
 340 345 350
 Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
 355 360 365
 Gly Glu Gly Thr Ser Thr Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly
 370 375 380
 Ala Asp Asp Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser
 385 390 395 400
 Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser
 405 410 415
 Tyr Met Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp
 420 425 430
 Ile Tyr Asp Thr Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser
 435 440 445
 Gly Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu
 450 455 460

Ala Glu Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro
 465 470 475 480

Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
 485 490

<210> 209

<211> 1476

<212> DNA

<213> artificial sequence

<220>

<223> CCR5xanti-CD3 VH5VL3

<400> 209

gacattatcc	tgatccaatc	tccaccttct	ttggctgtgt	ctctagggca	gagggccacc	60
atctcctgca	gaaccagcga	aatgttgac	ggatacggca	ttagttttat	aaactggtac	120
caacagaagc	caggacagcc	acccaaactc	ctcatctatg	ctgcatccca	ccaaggatcc	180
ggggtccttg	ccagatttag	tggcagtggg	tctgggacag	acttcagcct	caacatccat	240
cctttggagg	aggatgatac	tgcaatgtat	ttctgtcacc	aaagtaagaa	ggttccgtgg	300
acgttcggtg	gaggcaccaa	gctggaaatc	aaagggtggtg	gtggttcttg	cggcggcggc	360
tccggtggtg	gtggttctca	gctggagcag	tctggacctg	aactgaagaa	gcctggagag	420
acagtcacga	tctcctgcaa	ggcttctggg	tataccttca	cgaagttcgg	aatgaactgg	480
gtgaagcagg	ctccaggaaa	gggtttaaag	tggatgggct	ggatacacac	ctccactgga	540
gagccaacat	attctgatga	cttcaaggga	cggtttgcct	tctctttgga	aacgtctgcc	600
agcactgcct	atttgcggat	caacaacctc	aaaaatgagg	acatggctaa	atacttctgt	660
gccagaggtg	gtccttacgt	aaggggtgct	ttggactact	gggggtcaagg	aacctcagtc	720
accgtctcct	ccggaggtgg	tggatccgac	gtccaactgg	tgcagtcagg	ggctgaagtg	780
aaaaaacctg	gggcctcagt	gaagggtgtc	tgcaaggctt	ctggctacac	ctttactagg	840
tacacgatgc	actgggtaag	gcaggcacct	ggacagggtc	tggaatggat	tggatacatt	900
aatcctagcc	gtggttatac	taattacgca	gacagcgtca	agggccgctt	cacaatcact	960
acagacaaat	ccaccagcac	agcctacatg	gaactgagca	gcctgcgttc	tgaggacact	1020
gcaacctatt	actgtgcaag	atattatgat	gatcattact	gccttgacta	ctggggccaa	1080
ggcaccacgg	tcaccgtctc	ctcaggcgaa	ggtactagta	ctggttcttg	tggaagtgga	1140
ggttcaggtg	gagcagacga	cattgtactg	accagtcctc	cagcaactct	gtctctgtct	1200
ccaggggagc	gtgccaccct	gacctgcaga	gccagttcaa	gtgtaagtta	catgaactgg	1260
taccagcaga	agccgggcaa	ggcacccaaa	agatggattt	atgacacatc	caaagtggct	1320

tctggagtcc	ctgctcgctt	cagtggcagt	gggtctggga	ccgactactc	tctcacaatc	1380
aacagcttgg	aggctgaaga	tgctgccact	tattactgcc	aacagtggag	tagtaacccg	1440
ctcacgttcg	gtggcgggac	caaggtggag	atcaaaa			1476

<210> 210
 <211> 492
 <212> PRT
 <213> artificial sequence

<220>

<223> CCR5xanti-CD3 VH5VL3

<400> 210

Asp Ile Ile Leu Ile Gln Ser Pro Pro Ser Leu Ala Val ser Leu Gly
 1 5 10 15

Gln Arg Ala Thr Ile Ser Cys Arg Thr Ser Glu Asn Val Asp Gly Tyr
 20 25 30

Gly Ile Ser Phe Ile Asn Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro
 35 40 45

Lys Leu Leu Ile Tyr Ala Ala Ser His Gln Gly Ser Gly Val Pro Ala
 50 55 60

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Ser Leu Asn Ile His
 65 70 75 80

Pro Leu Glu Glu Asp Asp Thr Ala Met Tyr Phe Cys His Gln Ser Lys
 85 90 95

Lys Val Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Gly
 100 105 110

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Ser Gln Leu
 115 120 125

Glu Gln Ser Gly Pro Glu Leu Lys Lys Pro Gly Glu Thr Val Thr Ile
 130 135 140

Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Lys Phe Gly Met Asn Trp
 145 150 155 160

Val Lys Gln Ala Pro Gly Lys Gly Leu Lys Trp Met Gly Trp Ile His
 165 170 175

Thr Ser Thr Gly Glu Pro Thr Tyr Ser Asp Asp Phe Lys Gly Arg Phe
 180 185 190

Ala Phe Ser Leu Glu Thr Ser Ala Ser Thr Ala Tyr Leu Arg Ile Asn
 195 200 205
 Asn Leu Lys Asn Glu Asp Met Ala Lys Tyr Phe Cys Ala Arg Gly Gly
 210 215 220
 Pro Tyr Val Arg Gly Ala Leu Asp Tyr Trp Gly Gln Gly Thr Ser Val
 225 230 235 240
 Thr Val Ser Ser Gly Gly Gly Gly Ser Asp Val Gln Leu Val Gln Ser
 245 250 255
 Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys
 260 265 270
 Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp Val Arg Gln
 275 280 285
 Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn Pro Ser Arg
 290 295 300
 Gly Tyr Thr Asn Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Thr
 305 310 315 320
 Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg
 325 330 335
 Ser Glu Asp Thr Ala Thr Tyr Tyr Cys Ala Arg Tyr Tyr Asp Asp His
 340 345 350
 Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
 355 360 365
 Gly Glu Gly Thr Ser Thr Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly
 370 375 380
 Ala Asp Asp Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser
 385 390 395 400
 Pro Gly Glu Arg Ala Thr Leu Thr Cys Arg Ala Ser Ser Ser Val Ser
 405 410 415
 Tyr Met Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp
 420 425 430
 Ile Tyr Asp Thr Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser
 435 440 445
 Gly Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu
 450 455 460

Ala Glu Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro
 465 470 475 480

Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
 485 490

<210> 211

<211> 1476

<212> DNA

<213> artificial sequence

<220>

<223> CCR5xanti-CD3 VH7VL1

<400> 211

gacattatcc tgatccaatc tccaccttct ttggctgtgt ctctagggca gagggccacc	60
atctcctgca gaaccagcga aaatgttgac ggatacggca ttagttttat aaactggtac	120
caacagaagc caggacagcc acccaaactc ctcatctatg ctgcatccca ccaaggatcc	180
ggggtccttg ccagatttag tggcagtggg tctgggacag acttcagcct caacatccat	240
cctttggagg aggatgatac tgcaatgtat ttctgtcacc aaagtaagaa ggttccgtgg	300
acgttcggtg gaggcaccaa gctggaaatc aaagggtggtg gtggttcttg cggcggcggc	360
tccggtggtg gtggttctca gctggagcag tctggacctg aactgaagaa gcctggagag	420
acagtcacga tctcctgcaa ggcttctggg tataccttca cgaagttcgg aatgaactgg	480
gtgaagcagg ctccaggaaa gggtttaaaag tggatgggct ggatacacac ctccactgga	540
gagccaacat attctgatga cttcaaggga cggtttgcct tctctttgga aacgtctgcc	600
agcactgcct atttgcggat caacaacctc aaaaatgagg acatggctaa atacttctgt	660
gccagaggtg gtccttacgt aaggggtgct ttggactact ggggtcaagg aacctcagtc	720
accgtctcct ccggaggtgg tggatccgac gtccaactgg tgcagtcagg ggctgaagtg	780
aaaaaacctg gggcctcagt gaagggtgcc tgcaaggctt ctggctacac ctttactagg	840
tacacgatgc actgggtaag gcaggcacct ggacagggtc tggaatggat tggatacatt	900
aatcctagcc gtggttatac taattacaat cagaagtcca aggaccgcgt cacaatcact	960
acagacaaat ccaccagcac agcctacatg gaactgagca gcctgcgttc tgaggacact	1020
gcagtctatt actgtgcaag atattatgat gatcattact gccttgacta ctggggccaa	1080
ggcaccacgg tcaccgtctc ctcaggcgaa ggtactagta ctggttcttg tggaagtgga	1140
ggttcaggtg gagcagacga cattcagatg acccagtctc catctagcct gtctgcatct	1200
gtcggggacc gtgtcaccat cacctgcaga gccagtcaaa gtgtaagtta catgaactgg	1260
taccagcaga agccgggcaa ggcacccaaa agatggattt atgacacatc caaagtggct	1320
tctggagtcc ctgctcgctt cagtggcagt gggctctggga ccgactactc tctcacaatc	1380

aacagcttgg aggctgaaga tgctgccact tattactgcc aacagtggag tagtaaccgc 1440
ctcacgttcg gtggcgggac caaggtggag atcaaa 1476

<210> 212

<211> 492

<212> PRT

<213> artificial sequence

<220>

<223> CCR5xanti-CD3 VH7VL1

<400> 212

Asp Ile Ile Leu Ile Gln Ser Pro Pro Ser Leu Ala Val Ser Leu Gly
1 5 10 15

Gln Arg Ala Thr Ile Ser Cys Arg Thr Ser Glu Asn Val Asp Gly Tyr
20 25 30

Gly Ile Ser Phe Ile Asn Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro
35 40 45

Lys Leu Leu Ile Tyr Ala Ala Ser His Gln Gly Ser Gly Val Pro Ala
50 55 60

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Ser Leu Asn Ile His
65 70 75 80

Pro Leu Glu Glu Asp Asp Thr Ala Met Tyr Phe Cys His Gln Ser Lys
85 90 95

Lys Val Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Gly
100 105 110

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Leu
115 120 125

Glu Gln Ser Gly Pro Glu Leu Lys Lys Pro Gly Glu Thr Val Thr Ile
130 135 140

Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Lys Phe Gly Met Asn Trp
145 150 155 160

Val Lys Gln Ala Pro Gly Lys Gly Leu Lys Trp Met Gly Trp Ile His
165 170 175

Thr Ser Thr Gly Glu Pro Thr Tyr Ser Asp Asp Phe Lys Gly Arg Phe
180 185 190

Ala Phe Ser Leu Glu Thr Ser Ala Ser Thr Ala Tyr Leu Arg Ile Asn
 195 200 205

Asn Leu Lys Asn Glu Asp Met Ala Lys Tyr Phe Cys Ala Arg Gly Gly
 210 215 220

Pro Tyr Val Arg Gly Ala Leu Asp Tyr Trp Gly Gln Gly Thr Ser Val
 225 230 235 240

Thr Val Ser Ser Gly Gly Gly Gly Ser Asp Val Gln Leu Val Gln Ser
 245 250 255

Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys
 260 265 270

Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp Val Arg Gln
 275 280 285

Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn Pro Ser Arg
 290 295 300

Gly Tyr Thr Asn Tyr Asn Gln Lys Phe Lys Asp Arg Val Thr Ile Thr
 305 310 315 320

Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg
 325 330 335

Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Tyr Tyr Asp Asp His
 340 345 350

Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
 355 360 365

Gly Glu Gly Thr Ser Thr Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly
 370 375 380

Ala Asp Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser
 385 390 395 400

Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Ser
 405 410 415

Tyr Met Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp
 420 425 430

Ile Tyr Asp Thr Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser
 435 440 445

Gly Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu
 450 455 460

Ala Glu Asp Ala Ala Thr Tyr Tyr Cys Gln¹⁶³ Gln Trp Ser Ser Asn Pro
 465 470 475 480

Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
 485 490

<210> 213

<211> 1476

<212> DNA

<213> artificial sequence

<220>

<223> CCR5xanti-CD3 VH7VL2

<400> 213

gacattatcc	tgatccaatc	tccaccttct	ttggctgtgt	ctctagggca	gagggccacc	60
atctcctgca	gaaccagcga	aaatgttgac	ggatacggca	ttagttttat	aaactggtag	120
caacagaagc	caggacagcc	acccaaactc	ctcatctatg	ctgcatccca	ccaaggatcc	180
gggggccctg	ccagatttag	tggcagtggg	tctgggacag	acttcagcct	caacatccat	240
cctttggagg	aggatgatac	tgcaatgtat	ttctgtcacc	aaagtaagaa	ggttccgtgg	300
acgttcggtg	gaggcaccaa	gctggaaatc	aaaggtggtg	gtggttcttg	cggcggcggc	360
tccggtggtg	gtggttctca	gctggagcag	tctggacctg	aactgaagaa	gcctggagag	420
acagtcacga	tctcctgcaa	ggcttctggg	tataccttca	cgaagttcgg	aatgaactgg	480
gtgaagcagg	ctccaggaaa	gggttttaaag	tggatgggct	ggatacacac	ctccactgga	540
gagccaacat	attctgatga	cttcaaggga	cggtttgcct	tctctttgga	aacgtctgcc	600
agcactgcct	atttgcggat	caacaacctc	aaaaatgagg	acatggctaa	atacttctgt	660
gccagaggtg	gtccttacgt	aaggggtgct	ttggactact	gggggtcaagg	aacctcagtc	720
accgtctcct	ccggaggtgg	tggatccgac	gtccaactgg	tgcatgcagg	ggctgaagtg	780
aaaaaacctg	gggcctcagt	gaaggtgtcc	tgcaaggctt	ctggctacac	ctttactagg	840
tacacgatgc	actgggtaag	gcaggcacct	ggacagggtc	tggaatggat	tggatacatt	900
aatcctagcc	gtggttatac	taattacaat	cagaagttca	aggaccgcgt	cacaatcact	960
acagacaaat	ccaccagcac	agcctacatg	gaactgagca	gcctgcgttc	tgaggacact	1020
gcagtctatt	actgtgcaag	atattatgat	gatcattact	gccttgacta	ctggggccaa	1080
ggcaccacgg	tcaccgtctc	ctcaggcgaa	ggtactagta	ctggttcttg	tggaaagtga	1140
ggttcaggtg	gagcagacga	cattgtactg	accagtcctc	cagcaactct	gtctctgtct	1200
ccagggggagc	gtgccaccct	gagctgcaga	gccagtcaaa	gtgtaagtta	catgaactgg	1260
taccagcaga	agccggggcaa	ggcaccctaaa	agatggattt	atgacacatc	caaagtggct	1320
tctggagtcc	ctgctcgctt	cagtggcagt	gggtctggga	ccgactactc	tctcacaatc	1380

164
aacagcttgg aggctgaaga tgctgccact tattactgcc aacagtggag tagtaacccg 1440
ctcacgttcg gtggcgggac caaggtggag atcaaa 1476

<210> 214

<211> 492

<212> PRT

<213> artificial sequence

<220>

<223> CCR5xanti-CD3 VH7VL2

<400> 214

Asp Ile Ile Leu Ile Gln Ser Pro Pro Ser Leu Ala Val Ser Leu Gly
1 5 10 15

Gln Arg Ala Thr Ile Ser Cys Arg Thr Ser Glu Asn Val Asp Gly Tyr
20 25 30

Gly Ile Ser Phe Ile Asn Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro
35 40 45

Lys Leu Leu Ile Tyr Ala Ala Ser His Gln Gly Ser Gly Val Pro Ala
50 55 60

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Ser Leu Asn Ile His
65 70 75 80

Pro Leu Glu Glu Asp Asp Thr Ala Met Tyr Phe Cys His Gln Ser Lys
85 90 95

Lys Val Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Gly
100 105 110

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Leu
115 120 125

Glu Gln Ser Gly Pro Glu Leu Lys Lys Pro Gly Glu Thr Val Thr Ile
130 135 140

Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Lys Phe Gly Met Asn Trp
145 150 155 160

Val Lys Gln Ala Pro Gly Lys Gly Leu Lys Trp Met Gly Trp Ile His
165 170 175

Thr Ser Thr Gly Glu Pro Thr Tyr Ser Asp Asp Phe Lys Gly Arg Phe
180 185 190

Ala Phe Ser₁₉₅ Leu Glu Thr Ser Ala₂₀₀ Ser Thr¹⁶⁵ Ala Tyr Leu₂₀₅ Arg Ile Asn
 Asn Leu₂₁₀ Lys Asn Glu Asp Met₂₁₅ Ala Lys Tyr Phe Cys₂₂₀ Ala Arg Gly Gly
 Pro Tyr Val Arg Gly Ala₂₃₀ Leu Asp Tyr Trp Gly₂₃₅ Gln Gly Thr Ser Val₂₄₀
 Thr Val Ser Ser Gly₂₄₅ Gly Gly Gly Ser Asp₂₅₀ Val Gln Leu Val Gln Ser₂₅₅
 Gly Ala Glu Val₂₆₀ Lys Lys Pro Gly Ala₂₆₅ Ser Val Lys Val Ser₂₇₀ Cys Lys
 Ala Ser Gly₂₇₅ Tyr Thr Phe Thr Arg₂₈₀ Tyr Thr Met His Trp₂₈₅ Val Arg Gln
 Ala Pro₂₉₀ Gly Gln Gly Leu Glu₂₉₅ Trp Ile Gly Tyr Ile₃₀₀ Asn Pro Ser Arg
 Gly Tyr Thr Asn Tyr Asn₃₁₀ Gln Lys Phe Lys Asp₃₁₅ Arg Val Thr Ile Thr₃₂₀
 Thr Asp Lys Ser Thr₃₂₅ Ser Thr Ala Tyr Met₃₃₀ Glu Leu Ser Ser Leu₃₃₅ Arg
 Ser Glu Asp Thr₃₄₀ Ala Val Tyr Tyr Cys₃₄₅ Ala Arg Tyr Tyr Asp₃₅₀ Asp His
 Tyr Cys Leu₃₅₅ Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr₃₆₅ Val Ser Ser
 Gly Glu Gly Thr Ser Thr Gly₃₇₅ Ser Gly Gly Ser Gly₃₈₀ Gly Ser Gly Gly
 Ala Asp Asp Ile Val Leu₃₉₀ Thr Gln Ser Pro Ala₃₉₅ Thr Leu Ser Leu Ser₄₀₀
 Pro Gly Glu Arg Ala₄₀₅ Thr Leu Ser Cys Arg₄₁₀ Ala Ser Gln Ser Val₄₁₅ Ser
 Tyr Met Asn Trp₄₂₀ Tyr Gln Gln Lys Pro₄₂₅ Gly Lys Ala Pro Lys₄₃₀ Arg Trp
 Ile Tyr Asp₄₃₅ Thr Ser Lys Val Ala₄₄₀ Ser Gly Val Pro Ala₄₄₅ Arg Phe Ser
 Gly Ser Gly Ser Gly Thr Asp₄₅₅ Tyr Ser Leu Thr Ile₄₆₀ Asn Ser Leu Glu
 Ala Glu Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro

465

470

166
475

480

Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys

485490

<210> 215

<211> 1476

<212> DNA

<213> artificial sequence

<220>

<223> CCR5xanti-CD3 VH7VL3

<400> 215

gacattatcc

tgatccaatc

tccaccttct

ttggctgtgt

ctctagggca

gagggccacc

60

atctcctgca

gaaccagcga

aaatgttgac

ggatacggca

ttagttttat

aaactggtac

120

caacagaagc

caggacagcc

acccaaactc

ctcatctatg

ctgcatccca

ccaaggatcc

180

ggggtccttg

ccagatttag

tggcagtggg

tctgggacag

acttcagcct

caacatccat

240

cctttggagg

aggatgatac

tgcaatgtat

ttctgtcacc

aaagtaagaa

ggttccgtgg

300

acgttcggtg

gaggcaccaa

gctggaaatc

aaaggtggtg

gtggttctgg

cggcggcggc

360

tccggtggtg

gtggttctca

gctggagcag

tctggacctg

aactgaagaa

gcctggagag

420

acagtcacga

tctcctgcaa

ggcttctggg

tataccttca

cgaagttcgg

aatgaactgg

480

gtgaagcagg

ctccaggaaa

gggtttaaag

tggatgggct

ggatacacac

ctccactgga

540

gagccaacat

attctgatga

cttcaaggga

cggtttgcct

tctctttgga

aacgtctgcc

600

agcactgcct

atttgcggat

caacaacctc

aaaaatgagg

acatggctaa

atacttctgt

660

gccagaggtg

gtccttacgt

aaggggtgct

ttggactact

ggggtcaagg

aacctcagtc

720

accgtctcct

ccggaggtgg

tggatccgac

gtccaactgg

tgcagtcagg

ggctgaagtg

780

aaaaaacctg

gggcctcagt

gaaggtgtcc

tgcaaggctt

ctggctacac

ctttactagg

840

tacacgatgc

actgggtaag

gcaggcacct

ggacagggtc

tggaatggat

tggatacatt

900

aatcctagcc

gtggttatac

taattacaat

cagaagttca

aggaccgcgt

cacaatcact

960

acagacaaat

ccaccagcac

agcctacatg

gaactgagca

gcctgcgttc

tgaggacact

1020

gcagtctatt

actgtgcaag

atattatgat

gatcattact

gccttgacta

ctggggccaa

1080

ggcaccacgg

tcaccgtctc

ctcaggcgaa

ggtactagta

ctggttctgg

tggaagtgga

1140

ggttcaggtg

gagcagacga

cattgtactg

accagtctc

cagcaactct

gtctctgtct

1200

ccagggggagc

gtgccaccct

gacctgcaga

gccagttcaa

gtgtaagtta

catgaactgg

1260

taccagcaga

agccgggcaa

ggcacccaaa

agatggattt

atgacacatc

caaagtggct

1320

tctggagtcc

ctgctcgctt

cagtggcagt

gggtctggga

ccgactactc

tctcacaatc

1380

aacagcttgg

aggctgaaga

tgctgccact

tattactgcc

aacagtggag

tagtaacccg

1440

ctcacgttcg gtggcgggac caaggtggag atcaaa

1476

<210> 216

<211> 492

<212> PRT

<213> artificial sequence

<220>

<223> CCR5xanti-CD3 VH7VL3

<400> 216

Asp Ile Ile Leu Ile Gln Ser Pro Pro Ser Leu Ala Val Ser Leu Gly
1 5 10 15

Gln Arg Ala Thr Ile Ser Cys Arg Thr Ser Glu Asn Val Asp Gly Tyr
20 25 30

Gly Ile Ser Phe Ile Asn Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro
35 40 45

Lys Leu Leu Ile Tyr Ala Ala Ser His Gln Gly Ser Gly Val Pro Ala
50 55 60

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Ser Leu Asn Ile His
65 70 75 80

Pro Leu Glu Glu Asp Asp Thr Ala Met Tyr Phe Cys His Gln Ser Lys
85 90 95

Lys Val Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Gly
100 105 110

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Leu
115 120 125

Glu Gln Ser Gly Pro Glu Leu Lys Lys Pro Gly Glu Thr Val Thr Ile
130 135 140

Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Lys Phe Gly Met Asn Trp
145 150 155 160

Val Lys Gln Ala Pro Gly Lys Gly Leu Lys Trp Met Gly Trp Ile His
165 170 175

Thr Ser Thr Gly Glu Pro Thr Tyr Ser Asp Asp Phe Lys Gly Arg Phe
180 185 190

Ala Phe Ser Leu Glu Thr Ser Ala Ser Thr Ala Tyr Leu Arg Ile Asn

	195		200		168		205								
Asn	Leu	Lys	Asn	Glu	Asp	Met	Ala	Lys	Tyr	Phe	Cys	Ala	Arg	Gly	Gly
	210					215					220				
Pro	Tyr	Val	Arg	Gly	Ala	Leu	Asp	Tyr	Trp	Gly	Gln	Gly	Thr	Ser	Val
225					230					235					240
Thr	Val	Ser	Ser	Gly	Gly	Gly	Gly	Ser	Asp	Val	Gln	Leu	Val	Gln	Ser
				245					250					255	
Gly	Ala	Glu	Val	Lys	Lys	Pro	Gly	Ala	Ser	Val	Lys	Val	Ser	Cys	Lys
			260					265					270		
Ala	Ser	Gly	Tyr	Thr	Phe	Thr	Arg	Tyr	Thr	Met	His	Trp	Val	Arg	Gln
		275					280					285			
Ala	Pro	Gly	Gln	Gly	Leu	Glu	Trp	Ile	Gly	Tyr	Ile	Asn	Pro	Ser	Arg
	290					295					300				
Gly	Tyr	Thr	Asn	Tyr	Asn	Gln	Lys	Phe	Lys	Asp	Arg	Val	Thr	Ile	Thr
305					310					315					320
Thr	Asp	Lys	Ser	Thr	Ser	Thr	Ala	Tyr	Met	Glu	Leu	Ser	Ser	Leu	Arg
				325					330					335	
Ser	Glu	Asp	Thr	Ala	Val	Tyr	Tyr	Cys	Ala	Arg	Tyr	Tyr	Asp	Asp	His
			340					345					350		
Tyr	Cys	Leu	Asp	Tyr	Trp	Gly	Gln	Gly	Thr	Thr	Val	Thr	Val	Ser	Ser
		355					360					365			
Gly	Glu	Gly	Thr	Ser	Thr	Gly	Ser	Gly	Gly	Ser	Gly	Gly	Ser	Gly	Gly
	370					375					380				
Ala	Asp	Asp	Ile	Val	Leu	Thr	Gln	Ser	Pro	Ala	Thr	Leu	Ser	Leu	Ser
385					390					395					400
Pro	Gly	Glu	Arg	Ala	Thr	Leu	Thr	Cys	Arg	Ala	Ser	Ser	Ser	Val	Ser
				405					410					415	

Tyr	Met	Asn	Trp	Tyr	Gln	Gln	Lys	Pro	Gly	Lys	Ala	Pro	Lys	Arg	Trp
			420					425					430		
Ile	Tyr	Asp	Thr	Ser	Lys	Val	Ala	Ser	Gly	Val	Pro	Ala	Arg	Phe	Ser
		435					440					445			
Gly	Ser	Gly	Ser	Gly	Thr	Asp	Tyr	Ser	Leu	Thr	Ile	Asn	Ser	Leu	Glu
	450					455					460				
Ala	Glu	Asp	Ala	Ala	Thr	Tyr	Tyr	Cys	Gln	Gln	Trp	Ser	Ser	Asn	Pro
465					470					475					480

Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
 485 490

<210> 217

<211> 1473

<212> DNA

<213> artificial sequence

<220>

<223> CD20xanti-CD3 VH5VL1

<400> 217

caaattgttc tctcccagtc tccagcaatc ctttctgcat ctccagggga gaaggtcaca	60
atgacttgca gggccagctc aagtttaagt ttcatgcact ggtaccagca gaagccagga	120
tcctcccca aaccctggat ttatgccaca tccaacctgg cttctggagt ccctgctcgc	180
ttcagtgga gtgggtctgg gacctcttac tctctcacia tcagcagagt ggaggctgaa	240
gatgctgcca cttatttctg ccatcagtgg agtagtaacc cgctcacgtt cgggtgctggg	300
acaaagggtg aaataaaagg tgggtggtgg tctggcggcg gcggctccgg tgggtggtgg	360
tctcaggtgc aactgcggca gcctggggct gagctggtga agcctggggc ctcagtgaag	420
atgtcctgca aggcttctgg ctacacattt accagttaca atatgcactg ggtaaagcag	480
acacctggac agggcctgga atggattgga gctatttata caggaaatgg tgatacttcc	540
tacaatcaga agttcaaagg caaggccaca ttgactgcag acaaatcctc cagcacagcc	600
tacatgcagc tcagcagtct gacatctgag gactctgcgg tctattactg tgcaagatcg	660
cactacggta gtaactacgt agactacttt gactactggg gccaaaggcac actagtcaca	720
gtctcgacag gaggtggtgg atccgacgtc caactggtgc agtcaggggc tgaagtga	780
aaacctgggg cctcagtga ggtgtcctgc aaggcttctg gctacacctt tactaggtac	840
acgatgcact gggtaaggca ggcacctgga cagggtctgg aatggattgg atacattaat	900
cctagccgtg gttatactaa ttacgcagac agcgtcaagg gccgcttcac aatcactaca	960
gacaaatcca ccagcacagc ctacatggaa ctgagcagcc tgcgttctga ggacactgca	1020
acctattact gtgcaagata ttatgatgat cattactgcc ttgactactg gggccaaggc	1080
accacggtca ccgtctcctc aggcgaagggt actagtactg gttctgggtgg aagtggaggt	1140
tcaggtggag cagacgacat tcagatgacc cagtctccat ctagcctgtc tgcattctgtc	1200
ggggaccgtg tcaccatcac ctgcagagcc agtcaaagtg taagttacat gaactgggtac	1260
cagcagaagc cgggcaaggc acccaaaaga tggatttatg acacatccaa agtggccttct	1320
ggagtccttg ctgccttcag tggcagtggtg tctgggaccg actactctct cacaatcaac	1380
agcttgaggg ctgaagatgc tgccacttat tactgccaac agtggagtag taaccgctc	1440

acgttcggtg gcgggaccaa ggtggagatc aaa 170

1473

<210> 218

<211> 491

<212> PRT

<213> artificial sequence

<220>

<223> CD20xanti-CD3 VH5VL1

<400> 218

Gln Ile Val Leu Ser Gln Ser Pro Ala Ile Leu Ser Ala Ser Pro Gly
1 5 10 15

Glu Lys Val Thr Met Thr Cys Arg Ala Ser Ser Ser Leu Ser Phe Met
20 25 30

His Trp Tyr Gln Gln Lys Pro Gly Ser Ser Pro Lys Pro Trp Ile Tyr
35 40 45

Ala Thr Ser Asn Leu Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
50 55 60

Gly Ser Gly Thr Ser Tyr Ser Leu Thr Ile Ser Arg Val Glu Ala Glu
65 70 75 80

Asp Ala Ala Thr Tyr Phe Cys His Gln Trp Ser Ser Asn Pro Leu Thr
85 90 95

Phe Gly Ala Gly Thr Lys Val Glu Ile Lys Gly Gly Gly Gly Ser Gly
100 105 110

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Val Gln Leu Arg Gln Pro
115 120 125

Gly Ala Glu Leu Val Lys Pro Gly Ala Ser Val Lys Met Ser Cys Lys
130 135 140

Ala Ser Gly Tyr Thr Phe Thr Ser Tyr Asn Met His Trp Val Lys Gln
145 150 155 160

Thr Pro Gly Gln Gly Leu Glu Trp Ile Gly Ala Ile Tyr Pro Gly Asn
165 170 175

Gly Asp Thr Ser Tyr Asn Gln Lys Phe Lys Gly Lys Ala Thr Leu Thr
180 185 190

Ala Asp Lys Ser Ser Ser Thr Ala Tyr Met Gln Leu Ser Ser Leu Thr
195 200 205

Ser Glu Asp Ser Ala Val Tyr Tyr Cys Ala Arg Ser His Tyr Gly Ser
 210 215 220
 Asn Tyr Val Asp Tyr Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr
 225 230 235 240
 Val Ser Thr Gly Gly Gly Gly Ser Asp Val Gln Leu Val Gln Ser Gly
 245 250 255
 Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala
 260 265 270
 Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp Val Arg Gln Ala
 275 280 285
 Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn Pro Ser Arg Gly
 290 295 300
 Tyr Thr Asn Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Thr Thr
 305 310 315 320
 Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg Ser
 325 330 335
 Glu Asp Thr Ala Thr Tyr Tyr Cys Ala Arg Tyr Tyr Asp Asp His Tyr
 340 345 350
 Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly
 355 360 365
 Glu Gly Thr Ser Thr Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly Ala
 370 375 380
 Asp Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val
 385 390 395 400
 Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Ser Tyr
 405 410 415
 Met Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile
 420 425 430
 Tyr Asp Thr Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly
 435 440 445
 Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala
 450 455 460
 Glu Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu
 465 470 475 480

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
 485 490

<210> 219

<211> 1473

<212> DNA

<213> artificial sequence

<220>

<223> CD20xanti-CD3 VH5VL2

<400> 219

caaattgttc tctcccagtc tccagcaatc ctttctgcat ctccagggga gaaggtcaca	60
atgacttgca gggccagctc aagtttaagt ttcatgcact ggtaccagca gaagccagga	120
tctccccca aaccctggat ttatgccaca tccaacctgg cttctggagt ccctgctcgc	180
ttcagtggca gtgggtctgg gacctcttac tctctcacia tcagcagagt ggaggctgaa	240
gatgctgcca cttatttctg ccatcagtgg agtagtaacc cgctcacgtt cggtgctggg	300
acaaagggtg aaataaaagg tgggtggtggt tctggcggcg gcggctccgg tgggtggtggt	360
tctcaggtgc aactgcggca gcctggggct gagctggtga agcctggggc ctcagtgaag	420
atgtcctgca aggcttctgg ctacacattt accagttaca atatgcactg ggtaaagcag	480
acacctggac agggcctgga atggattgga gctatttatc caggaaatgg tgatacttcc	540
tacaatcaga agttcaaagg caaggccaca ttgactgcag acaaatcctc cagcacagcc	600
tacatgcagc tcagcagtct gacatctgag gactctgcgg tctattactg tgcaagatcg	660
cactacggta gtaactacgt agactacttt gactactggg gccaaaggcac actagtcaca	720
gtctcgacag gaggtggtgg atccgacgtc caactggtgc agtcaggggc tgaagtgaaa	780
aaacctgggg cctcagtga ggtgtcctgc aaggcttctg gctacacctt tactaggtac	840
acgatgcact gggtaaggca ggcacctgga cagggtctgg aatggattgg atacattaat	900
cctagccgtg gttatactaa ttacgcagac agcgtcaagg gccgcttcac aatcactaca	960
gacaaatcca ccagcacagc ctacatggaa ctgagcagcc tgcgttctga ggacactgca	1020
acctattact gtgcaagata ttatgatgat cattactgcc ttgactactg gggccaaggc	1080
accacgggtca ccgtctcctc aggcgaagggt actagtactg gttctggtgg aagtggaggt	1140
tcagggtggag cagacgacat tgtactgacc cagtctccag caactctgtc tctgtctcca	1200
ggggagcgtg ccacctgag ctgcagagcc agtcaaagtg taagttacat gaactgggtac	1260
cagcagaagc cgggcaaggc acccaaaaga tggatttatg acacatccaa agtggcttct	1320
ggagtccctg ctcgcttcag tggcagtggg tctgggaccg actactctct cacaatcaac	1380
agcttggagg ctgaagatgc tgccacttat tactgccaac agtggagtag taacccgctc	1440
acgttcggtg gcgggaccaa ggtggagatc aaa	1473

<210> 220
 <211> 491
 <212> PRT
 <213> artificial sequence

<220>

<223> CD20xanti-CD3 VH5VL2

<400> 220

Gln Ile Val Leu Ser Gln Ser Pro Ala Ile Leu Ser Ala Ser Pro Gly
 1 5 10 15

Glu Lys Val Thr Met Thr Cys Arg Ala Ser Ser Ser Leu Ser Phe Met
 20 25 30

His Trp Tyr Gln Gln Lys Pro Gly Ser Ser Pro Lys Pro Trp Ile Tyr
 35 40 45

Ala Thr Ser Asn Leu Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
 50 55 60

Gly Ser Gly Thr Ser Tyr Ser Leu Thr Ile Ser Arg Val Glu Ala Glu
 65 70 75 80

Asp Ala Ala Thr Tyr Phe Cys His Gln Trp Ser Ser Asn Pro Leu Thr
 85 90 95

Phe Gly Ala Gly Thr Lys Val Glu Ile Lys Gly Gly Gly Gly Ser Gly
 100 105 110

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Val Gln Leu Arg Gln Pro
 115 120 125

Gly Ala Glu Leu Val Lys Pro Gly Ala Ser Val Lys Met Ser Cys Lys
 130 135 140

Ala Ser Gly Tyr Thr Phe Thr Ser Tyr Asn Met His Trp Val Lys Gln
 145 150 155 160

Thr Pro Gly Gln Gly Leu Glu Trp Ile Gly Ala Ile Tyr Pro Gly Asn
 165 170 175

Gly Asp Thr Ser Tyr Asn Gln Lys Phe Lys Gly Lys Ala Thr Leu Thr
 180 185 190

Ala Asp Lys Ser Ser Ser Thr Ala Tyr Met Gln Leu Ser Ser Leu Thr
 195 200 205

Ser Glu Asp Ser Ala Val Tyr Tyr Cys Ala Arg Ser His Tyr Gly Ser
210 215 220

Asn Tyr Val Asp Tyr Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr
225 230 235 240

Val Ser Thr Gly Gly Gly Gly Ser Asp Val Gln Leu Val Gln Ser Gly
245 250 255

Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala
260 265 270

Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp Val Arg Gln Ala
275 280 285

Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn Pro Ser Arg Gly
290 295 300

Tyr Thr Asn Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Thr Thr
305 310 315 320

Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg Ser
325 330 335

Glu Asp Thr Ala Thr Tyr Tyr Cys Ala Arg Tyr Tyr Asp Asp His Tyr
340 345 350

Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly
355 360 365

Glu Gly Thr Ser Thr Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly Ala
370 375 380

Asp Asp Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro
385 390 395 400

Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Tyr
405 410 415

Met Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile
420 425 430

Tyr Asp Thr Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly
435 440 445

Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala
450 455 460

Glu Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu
465 470 475 480

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
485 175 490

<210> 221

<211> 1473

<212> DNA

<213> artificial sequence

<220>

<223> CD20xanti-CD3 VH5VL3

<400> 221

caaattgttc tctcccagtc tccagcaatc ctttctgcat ctccagggga gaaggtcaca	60
atgacttgca gggccagctc aagtttaagt ttcatgcact ggtaccagca gaagccagga	120
tcctcccca aaccctggat ttatgccaca tccaacctgg cttctggagt ccctgctcgc	180
ttcagtggca gtgggtctgg gacctcttac tctctcacia tcagcagagt ggaggctgaa	240
gatgctgcca cttatttctg ccatcagtgg agtagtaacc cgctcacgtt cggtgctggg	300
acaaagggtg aaataaaagg tgggtgggtg tctggcgggc gcggctccgg tgggtgggtg	360
tctcagggtg aactgcggca gcctggggct gagctgggtga agcctggggc ctcagtgaag	420
atgtcctgca aggcttctgg ctacacattt accagttaca atatgcactg ggtaaagcag	480
acacctggac agggcctgga atggattgga gctatttatt caggaaatgg tgatacttcc	540
tacaatcaga agttcaaagg caaggccaca ttgactgcag acaaatcctc cagcacagcc	600
tacatgcagc tcagcagtct gacatctgag gactctgcgg tctattactg tgcaagatcg	660
cactacggta gtaactacgt agactacttt gactactggg gccaaaggcac actagtcaca	720
gtctcgacag gaggtgggtg atccgacgtc caactgggtg agtcaggggc tgaagtgaag	780
aaacctgggg cctcagtga ggtgtcctgc aaggcttctg gctacacctt tactaggtac	840
acgatgcact gggtaaggca ggcacctgga cagggtctgg aatggattgg atacattaat	900
cctagccgtg gttatactaa ttacgcagac agcgtcaagg gccgcttcac aatcactaca	960
gacaaatcca ccagcacagc ctacatggaa ctgagcagcc tgcgttctga ggacactgca	1020
acctattact gtgcaagata ttatgatgat cattactgcc ttgactactg gggccaaggc	1080
accacgggtc ccgtctcctc aggcgaagggt actagtactg gttctgggtg aagtggagggt	1140
tcagggtggag cagacgacat tgtactgacc cagtctccag caactctgtc tctgtctcca	1200
ggggagcgtg ccaccctgac ctgcagagcc agttcaagtg taagttacat gaactgggtac	1260
cagcagaagc cgggcaaggc acccaaaaga tggatttatg acacatccaa agtggcttct	1320
ggagtccctg ctcgcttcag tggcagtggg tctgggaccg actactctct cacaatcaac	1380
agcttggagg ctgaagatgc tgccacttat tactgccaac agtggagtag taacccgctc	1440
acgttcggtg gcgggaccaa ggtggagatc aaa	1473

<210> 222

<211> 491

<212> PRT

<213> artificial sequence

<220>

<223> CD20xanti-CD3 VH5VL3

<400> 222

Gln Ile Val Leu Ser Gln Ser Pro Ala Ile Leu Ser Ala Ser Pro Gly
 1 5 10 15

Glu Lys Val Thr Met Thr Cys Arg Ala Ser Ser Ser Leu Ser Phe Met
 20 25 30

His Trp Tyr Gln Gln Lys Pro Gly Ser Ser Pro Lys Pro Trp Ile Tyr
 35 40 45

Ala Thr Ser Asn Leu Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
 50 55 60

Gly Ser Gly Thr Ser Tyr Ser Leu Thr Ile Ser Arg Val Glu Ala Glu
 65 70 75 80

Asp Ala Ala Thr Tyr Phe Cys His Gln Trp Ser Ser Asn Pro Leu Thr
 85 90 95

Phe Gly Ala Gly Thr Lys Val Glu Ile Lys Gly Gly Gly Gly Ser Gly
 100 105 110

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Val Gln Leu Arg Gln Pro
 115 120 125

Gly Ala Glu Leu Val Lys Pro Gly Ala Ser Val Lys Met Ser Cys Lys
 130 135 140

Ala Ser Gly Tyr Thr Phe Thr Ser Tyr Asn Met His Trp Val Lys Gln
 145 150 155 160

Thr Pro Gly Gln Gly Leu Glu Trp Ile Gly Ala Ile Tyr Pro Gly Asn
 165 170 175

Gly Asp Thr Ser Tyr Asn Gln Lys Phe Lys Gly Lys Ala Thr Leu Thr
 180 185 190

Ala Asp Lys Ser Ser Ser Thr Ala Tyr Met Gln Leu Ser Ser Leu Thr
 195 200 205

Ser Glu Asp Ser Ala Val Tyr Tyr Cys Ala Arg¹⁷⁷ Ser His Tyr Gly Ser
 210 215 220

Asn Tyr Val Asp Tyr Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr
 225 230 235 240

Val Ser Thr Gly Gly Gly Gly Ser Asp Val Gln Leu Val Gln Ser Gly
 245 250 255

Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala
 260 265 270

Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp Val Arg Gln Ala
 275 280 285

Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn Pro Ser Arg Gly
 290 295 300

Tyr Thr Asn Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Thr Thr
 305 310 315 320

Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg Ser
 325 330 335

Glu Asp Thr Ala Thr Tyr Tyr Cys Ala Arg Tyr Tyr Asp Asp His Tyr
 340 345 350

Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly
 355 360 365

Glu Gly Thr Ser Thr Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly Ala
 370 375 380

Asp Asp Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro
 385 390 395 400

Gly Glu Arg Ala Thr Leu Thr Cys Arg Ala Ser Ser Ser Val Ser Tyr
 405 410 415

Met Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile
 420 425 430

Tyr Asp Thr Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly
 435 440 445

Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala
 450 455 460

Glu Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu
 465 470 475 480

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys

<210> 223
<211> 1473
<212> DNA
<213> artificial sequence

<220>

<223> CD20xanti-CD3 VH7VL1

<400> 223
caaattgttc tctcccagtc tccagcaatc ctttctgcat ctccagggga gaaggtcaca 60
atgacttgca gggccagctc aagtttaagt ttcatgcact ggtaccagca gaagccagga 120
tcctcccca aaccctggat ttatgccaca tccaacctgg cttctggagt ccctgctcgc 180
ttcagtggca gtgggtctgg gacctcttac tctctcacia tcagcagagt ggaggctgaa 240
gatgctgcca cttatttctg ccatcagtgg agtagtaacc cgctcacgtt cggtgctggg 300
acaaaggtgg aaataaaagg tgggtgggtg tctggcggcg gcggctccgg tgggtgggtg 360
tctcaggtgc aactgcggca gcctggggct gagctgggtga agcctggggc ctcagtgaag 420
atgtcctgca aggcttctgg ctacacattt accagttaca atatgcactg ggtaaagcag 480
acacctggac agggcctgga atggattgga gctatttatc caggaaatgg tgatacttcc 540
tacaatcaga agttcaaagg caaggccaca ttgactgcag acaaatcctc cagcacagcc 600
tacatgcagc tcagcagtct gacatctgag gactctgcgg tctattactg tgcaagatcg 660
cactacggta gtaactacgt agactacttt gactactggg gccaaggcac actagtcaca 720
gtctcgacag gaggtgggtg atccgacgtc caactgggtg agtcaggggc tgaagtgaag 780
aaacctgggg cctcagtga ggtgtcctgc aaggcttctg gctacacctt tactaggtac 840
acgatgcact gggtaaggca ggcacctgga cagggtctgg aatggattgg atacattaat 900
cctagccgtg gttatactaa ttacaatcag aagttcaagg accgcgtcac aatcactaca 960
gacaaatcca ccagcacagc ctacatggaa ctgagcagcc tgcgttctga ggacactgca 1020
gtctattact gtgcaagata ttatgatgat cattactgcc ttgactactg gggccaaggc 1080
accacggtca ccgtctcctc aggcgaaggc actagtactg gttctgggtg aagtggaggt 1140
tcaggtggag cagacgacat tcagatgacc cagtctccat ctacgctgtc tgcattctgtc 1200
ggggaccgtg tcaccatcac ctgcagagcc agtcaaagtg taagttacat gaactgggtac 1260
cagcagaagc cgggcaaggc acccaaaaga tggatttatg acacatccaa agtggcttct 1320
ggagtccctg ctgcgttcag tggcagtggg tctgggaccg actactctct cacaatcaac 1380
agcttggagg ctgaagatgc tgccacttat tactgccaac agtggagtag taaccgctc 1440
acgttcggtg gcgggaccaa ggtggagatc aaa 1473

<210> 224

<211> 491

<212> PRT

<213> artificial sequence

<220>

<223> CD20xanti-CD3 VH7VL1

<400> 224

Gln Ile Val Leu Ser Gln Ser Pro Ala Ile Leu Ser Ala Ser Pro Gly
1 5 10 15

Glu Lys Val Thr Met Thr Cys Arg Ala Ser Ser Ser Leu Ser Phe Met
20 25 30

His Trp Tyr Gln Gln Lys Pro Gly Ser Ser Pro Lys Pro Trp Ile Tyr
35 40 45

Ala Thr Ser Asn Leu Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
50 55 60

Gly Ser Gly Thr Ser Tyr Ser Leu Thr Ile Ser Arg Val Glu Ala Glu
65 70 75 80

Asp Ala Ala Thr Tyr Phe Cys His Gln Trp Ser Ser Asn Pro Leu Thr
85 90 95

Phe Gly Ala Gly Thr Lys Val Glu Ile Lys Gly Gly Gly Gly Ser Gly
100 105 110

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Val Gln Leu Arg Gln Pro
115 120 125

Gly Ala Glu Leu Val Lys Pro Gly Ala Ser Val Lys Met Ser Cys Lys
130 135 140

Ala Ser Gly Tyr Thr Phe Thr Ser Tyr Asn Met His Trp Val Lys Gln
145 150 155 160

Thr Pro Gly Gln Gly Leu Glu Trp Ile Gly Ala Ile Tyr Pro Gly Asn
165 170 175

Gly Asp Thr Ser Tyr Asn Gln Lys Phe Lys Gly Lys Ala Thr Leu Thr
180 185 190

Ala Asp Lys Ser Ser Ser Thr Ala Tyr Met Gln Leu Ser Ser Leu Thr
195 200 205

Ser Glu Asp Ser Ala Val Tyr Tyr Cys Ala Arg Ser His Tyr Gly Ser

210	215	180	220
-----	-----	-----	-----

Asn Tyr Val Asp Tyr Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr
 225 230 235 240

Val ser Thr Gly Gly Gly Gly Ser Asp Val Gln Leu Val Gln Ser Gly
 245 250 255

Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala
 260 265 270

ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp Val Arg Gln Ala
 275 280 285

Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn Pro Ser Arg Gly
 290 295 300

Tyr Thr Asn Tyr Asn Gln Lys Phe Lys Asp Arg Val Thr Ile Thr Thr
 305 310 315 320

Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg Ser
 325 330 335

Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Tyr Tyr Asp Asp His Tyr
 340 345 350

Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly
 355 360 365

Glu Gly Thr Ser Thr Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly Ala
 370 375 380

Asp Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val
 385 390 395 400

Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Ser Tyr
 405 410 415

Met Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile
 420 425 430

Tyr Asp Thr Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly
 435 440 445

Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala
 450 455 460

Glu Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu
 465 470 475 480

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
 485 490

<210> 225

<211> 1473

<212> DNA

<213> artificial sequence

<220>

<223> CD20xanti-CD3 VH7VL2

<400> 225

caaattgttc tctcccagtc tccagcaatc ctttctgcat ctccagggga gaaggtcaca	60
atgacttgca gggccagctc aagtttaagt ttcatgcact ggtaccagca gaagccagga	120
tcttccccca aaccctggat ttatgccaca tccaacctgg cttctggagt ccctgctcgc	180
ttcagtgga gtgggtctgg gacctcttac tctctcacia tcagcagagt ggaggctgaa	240
gatgctgcca cttatttctg ccatcagtg agtagtaacc cgctcacgtt cgggtgctggg	300
acaaagggtg aaataaaagg tgggtggtgg tctggcggcg gcggctccgg tgggtggtgg	360
tctcaggtgc aactgcggca gcctggggct gagctggtga agcctggggc ctcagtgaag	420
atgtcctgca aggcttctgg ctacacattt accagttaca atatgcactg ggtaaagcag	480
acacctggac agggcctgga atggattgga gctatttatc caggaaatgg tgatacttcc	540
tacaatcaga agttcaaagg caaggccaca ttgactgcag acaaatcctc cagcacagcc	600
tacatgcagc tcagcagtct gacatctgag gactctgcgg tctattactg tgcaagatcg	660
cactacggta gtaactacgt agactacttt gactactggg gccaaaggcac actagtcaca	720
gtctcgacag gaggtggtgg atccgacgtc caactggtgc agtcaggggc tgaagtga	780
aaacctgggg cctcagtga ggtgtcctgc aaggcttctg gctacacctt tactaggtac	840
acgatgcact gggtaaaggca ggcacctgga cagggtctgg aatggattgg atacattaat	900
cctagccgtg gttatactaa ttacaatcag aagttcaagg accgcgtcac aatcactaca	960
gacaaatcca ccagcacagc ctacatggaa ctgagcagcc tgcgttctga ggacactgca	1020
gtctattact gtgcaagata ttatgatgat cattactgcc ttgactactg gggccaaggc	1080
accacgggtca ccgtctcctc aggcgaagggt actagtactg gttctgggtgg aagtggagggt	1140
tcagggtggag cagacgacat tgtactgacc cagtctccag caactctgtc tctgtctcca	1200
ggggagcgtg ccaccctgag ctgcagagcc agtcaaagtg taagttacat gaactggtac	1260
cagcagaagc cgggcaaggc acccaaaaga tggatttatg acacatccaa agtggcttct	1320
ggagtccctg ctcgcttcag tggcagtggtg tctgggaccg actactctct cacaatcaac	1380
agcttgagggt ctgaagatgc tgccacttat tactgccaac agtggagtag taacccgctc	1440
acgttcgggtg gcgggaccaa ggtggagatc aaa	1473

<210> 226

<211> 491

<212> PRT

<213> artificial sequence

<220>

<223> CD20xanti-CD3 VH7VL2

<400> 226

Gln Ile Val Leu Ser Gln Ser Pro Ala Ile Leu Ser Ala Ser Pro Gly
 1 5 10 15

Glu Lys Val Thr Met Thr Cys Arg Ala Ser Ser Ser Leu Ser Phe Met
 20 25 30

His Trp Tyr Gln Gln Lys Pro Gly Ser Ser Pro Lys Pro Trp Ile Tyr
 35 40 45

Ala Thr Ser Asn Leu Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
 50 55 60

Gly Ser Gly Thr Ser Tyr Ser Leu Thr Ile Ser Arg Val Glu Ala Glu
 65 70 75 80

Asp Ala Ala Thr Tyr Phe Cys His Gln Trp Ser Ser Asn Pro Leu Thr
 85 90 95

Phe Gly Ala Gly Thr Lys Val Glu Ile Lys Gly Gly Gly Gly Ser Gly
 100 105 110

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Val Gln Leu Arg Gln Pro
 115 120 125

Gly Ala Glu Leu Val Lys Pro Gly Ala Ser Val Lys Met Ser Cys Lys
 130 135 140

Ala Ser Gly Tyr Thr Phe Thr Ser Tyr Asn Met His Trp Val Lys Gln
 145 150 155 160

Thr Pro Gly Gln Gly Leu Glu Trp Ile Gly Ala Ile Tyr Pro Gly Asn
 165 170 175

Gly Asp Thr Ser Tyr Asn Gln Lys Phe Lys Gly Lys Ala Thr Leu Thr
 180 185 190

Ala Asp Lys Ser Ser Ser Thr Ala Tyr Met Gln Leu Ser Ser Leu Thr
 195 200 205

Ser Glu Asp Ser Ala Val Tyr Tyr Cys Ala Arg Ser His Tyr Gly Ser
 210 215 220

Asn Tyr Val Asp Tyr Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr
 225 230 235 240
 Val Ser Thr Gly Gly Gly Gly Ser Asp Val Gln Leu Val Gln Ser Gly
 245 250 255
 Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala
 260 265 270
 Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp Val Arg Gln Ala
 275 280 285
 Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn Pro Ser Arg Gly
 290 295 300
 Tyr Thr Asn Tyr Asn Gln Lys Phe Lys Asp Arg Val Thr Ile Thr Thr
 305 310 315 320
 Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg Ser
 325 330 335
 Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Tyr Tyr Asp Asp His Tyr
 340 345 350
 Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly
 355 360 365
 Glu Gly Thr Ser Thr Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly Ala
 370 375 380
 Asp Asp Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro
 385 390 395 400
 Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Tyr
 405 410 415
 Met Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile
 420 425 430
 Tyr Asp Thr Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly
 435 440 445
 Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala
 450 455 460
 Glu Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu
 465 470 475 480
 Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
 485 490

<210> 227

<211> 1473

<212> DNA

<213> artificial sequence

<220>

<223> CD20xanti-CD3 VH7VL3

<400> 227

caaattgttc tctcccagtc tccagcaatc ctttctgcat ctccagggga gaaggtcaca	60
atgacttgca gggccagctc aagttaagt ttcatgcact ggtaccagca gaagccagga	120
tcctcccca aaccctggat ttatgccaca tccaacctgg cttctggagt ccctgctcgc	180
ttcagtggca gtgggtctgg gacctcttac tctctcaca tcagcagagt ggaggctgaa	240
gatgctgcca cttatttctg ccatcagtgg agtagtaacc cgctcacgtt cggtgctggg	300
acaaagggtgg aaataaaagg tgggtggtggt tctggcggcg gcggctccgg tgggtggtggt	360
tctcagggtgc aactgcggca gcctggggct gagctggtga agcctggggc ctcagtgaag	420
atgtcctgca aggcttctgg ctacacattt accagttaca atatgcactg ggtaaagcag	480
acacctggac agggcctgga atggattgga gctatttatc caggaaatgg tgatacttcc	540
tacaatcaga agttcaaagg caaggccaca ttgactgcag acaaatcctc cagcacagcc	600
tacatgcagc tcagcagtct gacatctgag gactctgcgg tctattactg tgcaagatcg	660
cactacggta gtaactacgt agactacttt gactactggg gccaaggcac actagtcaca	720
gtctcgacag gaggtggtgg atccgacgtc caactggtgc agtcaggggc tgaagtgaaa	780
aaacctgggg cctcagtga ggtgtcctgc aaggcttctg gctacacctt tactaggtac	840
acgatgcact gggtaaggca ggcacctgga cagggtctgg aatggattgg atacattaat	900
cctagccgtg gttatactaa ttacaatcag aagttcaagg accgcgtcac aatcactaca	960
gacaaatcca ccagcacagc ctacatggaa ctgagcagcc tgcgttctga ggacactgca	1020
gtctattact gtgcaagata ttatgatgat cattactgcc ttgactactg gggccaaggc	1080
accacggtca ccgtctcctc aggcgaagggt actagtactg gttctggtgg aagtggaggt	1140
tcagggtggag cagacgacat tgtactgacc cagtctccag caactctgtc tctgtctcca	1200
ggggagcgtg ccacctgac ctgcagagcc agttcaagtg taagttacat gaactggtac	1260
cagcagaagc cgggcaaggc acccaaaaga tggatttatg acacatccaa agtggcttct	1320
ggagtccctg ctcgcttcag tggcagtggg tctgggaccg actactctct cacaatcaac	1380
agcttgaggg ctgaagatgc tgccacttat tactgccaac agtggagtag taaccgctc	1440
acgttcggtg gcgggaccaa ggtggagatc aaa	1473

<210> 228

<211> 491

<212> PRT

<213> artificial sequence

<220>

<223> CD20xanti-CD3 VH7VL3

<400> 228

Gln Ile Val Leu Ser Gln Ser Pro Ala Ile Leu Ser Ala Ser Pro Gly
 1 5 10 15

Glu Lys Val Thr Met Thr Cys Arg Ala Ser Ser Ser Leu Ser Phe Met
 20 25 30

His Trp Tyr Gln Gln Lys Pro Gly Ser Ser Pro Lys Pro Trp Ile Tyr
 35 40 45

Ala Thr Ser Asn Leu Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
 50 55 60

Gly Ser Gly Thr Ser Tyr Ser Leu Thr Ile Ser Arg Val Glu Ala Glu
 65 70 75 80

Asp Ala Ala Thr Tyr Phe Cys His Gln Trp Ser Ser Asn Pro Leu Thr
 85 90 95

Phe Gly Ala Gly Thr Lys Val Glu Ile Lys Gly Gly Gly Gly Ser Gly
 100 105 110

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Val Gln Leu Arg Gln Pro
 115 120 125

Gly Ala Glu Leu Val Lys Pro Gly Ala Ser Val Lys Met Ser Cys Lys
 130 135 140

Ala Ser Gly Tyr Thr Phe Thr Ser Tyr Asn Met His Trp Val Lys Gln
 145 150 155 160

Thr Pro Gly Gln Gly Leu Glu Trp Ile Gly Ala Ile Tyr Pro Gly Asn
 165 170 175

Gly Asp Thr Ser Tyr Asn Gln Lys Phe Lys Gly Lys Ala Thr Leu Thr
 180 185 190

Ala Asp Lys Ser Ser Ser Thr Ala Tyr Met Gln Leu Ser Ser Leu Thr
 195 200 205

Ser Glu Asp Ser Ala Val Tyr Tyr Cys Ala Arg Ser His Tyr Gly Ser
 210 215 220

Asn Tyr Val Asp Tyr Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr
225 230 235 240

Val Ser Thr Gly Gly Gly Gly Ser Asp Val Gln Leu Val Gln Ser Gly
245 250 255

Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala
260 265 270

Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp Val Arg Gln Ala
275 280 285

Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn Pro Ser Arg Gly
290 295 300

Tyr Thr Asn Tyr Asn Gln Lys Phe Lys Asp Arg Val Thr Ile Thr Thr
305 310 315 320

Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg Ser
325 330 335

Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Tyr Tyr Asp Asp His Tyr
340 345 350

Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly
355 360 365

Glu Gly Thr Ser Thr Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly Ala
370 375 380

Asp Asp Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro
385 390 395 400

Gly Glu Arg Ala Thr Leu Thr Cys Arg Ala Ser Ser Ser Val Ser Tyr
405 410 415

Met Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile
420 425 430

Tyr Asp Thr Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly
435 440 445

Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala
450 455 460

Glu Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu
465 470 475 480

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
485 490

<210> 229
 <211> 25
 <212> PRT
 <213> artificial sequence

<220>

<223> non-deimmunized anti-CD3 Framework 1

<400> 229

Asp Ile Lys Leu Gln Gln Ser Gly Ala Glu Leu Ala Arg Pro Gly Ala
 1 5 10 15

Ser Val Lys Met Ser Cys Lys Thr Ser
 20 25

<210> 230
 <211> 15
 <212> PRT
 <213> artificial sequence

<220>

<223> non-deimmunized anti-CD3 Framework 2

<400> 230

Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr
 1 5 10 15

<210> 231
 <211> 32
 <212> PRT
 <213> artificial sequence

<220>

<223> non-deimmunized anti-CD3 Framework 3

<400> 231

Lys Ala Thr Leu Thr Thr Asp Lys Ser Ser Ser Thr Ala Tyr Met Gln
 1 5 10 15

Leu Ser Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Tyr Cys Ala Arg
 20 25 30

<210> 232

<211> 11
 <212> PRT
 <213> artificial sequence

<220>
 <223> non-deimmunized anti-CD3 Framework 4
 <400> 232

Trp Gly Gln Gly Thr Thr Leu Thr Val Ser Ser
 1 5 10

<210> 233
 <211> 6
 <212> PRT
 <213> artificial sequence

<220>
 <223> sequence motif
 <400> 233

Ala Ser Gly Tyr Thr Phe
 1 5

<210> 234
 <211> 4
 <212> PRT
 <213> artificial sequence

<220>
 <223> sequence motif
 <400> 234

Met Glu Leu Ser
 1

<210> 235
 <211> 5
 <212> PRT
 <213> artificial sequence

<220>

<223> Sequence motif

<400> 235

Ile	Thr	Thr	Asp	Lys
1				5

<210> 236

<211> 1488

<212> DNA

<213> artificial sequence

<220>

<223> 5-10xVH5VL1 LHHL

<400> 236

gagctcgtga	tgacacagtc	tccatcctcc	ctgactgtga	cagcaggaga	gaaggctcact	60
atgagctgca	agtccagtca	gagtctgtta	aacagtggaa	atcaaaagaa	ctacttgacc	120
tggtaccagc	agaaaccagg	gcagcctcct	aaactgttga	tctactgggc	atccactagg	180
gaatctgggg	tccctgatcg	cttcacaggc	agtggatctg	gaacagattt	cactctcacc	240
atcagcagtg	tgaggctga	agacctggca	gtttattact	gtcagaatga	ttatagttat	300
ccgctcacgt	tcggtgctgg	gaccaagctt	gagatcaaag	gtggtggtgg	ttctggcggc	360
ggcggctccg	gtggtggtgg	ttctgaggtg	cagctgctcg	agcagtctgg	agctgagctg	420
gtaaggcctg	ggacttcagt	gaagatatcc	tgcaaggctt	ctggatacgc	cttcactaac	480
tactggctag	gttgggtaaa	gcagaggcct	ggacatggac	ttgagtggat	tggagatatt	540
ttccctggaa	gtggtaatat	ccactacaat	gagaagttca	agggcaaagc	cacactgact	600
gcagacaaat	cttcgagcac	agcctatatg	cagctcagta	gcctgacatt	tgaggactct	660
gctgtctatt	tctgtgcaag	actgaggaac	tgggacgagc	ctatggacta	ctggggccaa	720
gggaccacgg	tcaccgtctc	ctccggagggt	ggtggatccg	acgtccaact	ggtgcagtca	780
ggggctgaag	tgaaaaaacc	tggggcctca	gtgaagggtgt	cctgcaaggc	ttctggctac	840
acctttacta	ggtacacgat	gcactgggta	aggcaggcac	ctggacaggg	tctggaatgg	900
attggataca	ttaatcctag	ccgtggttat	actaattacg	cagacagcgt	caagggccgc	960
ttcacaatca	ctacagacaa	atccaccagc	acagcctaca	tggaaactgag	cagcctgcgt	1020
tctgaggaca	ctgcaaccta	ttactgtgca	agatattatg	atgatcatta	ctgccttgac	1080
tactggggcc	aaggcaccac	ggtcaccgtc	tcctcaggcg	aaggtagtag	tactggttct	1140
ggtggaagtg	gaggttcagg	tggagcagac	gacattcaga	tgaccagtc	tccatctagc	1200
ctgtctgcat	ctgtcgggga	ccgtgtcacc	atcacctgca	gagccagtca	aagtgtaagt	1260
tacatgaact	ggtaccagca	gaagccgggc	aaggcaccca	aaagatggat	ttatgacaca	1320

tccaaagtgg cttctggagt ccctgctcgc	190	gtgggtctgg gaccgactac	1380
tctctcacia tcaacagctt ggaggctgaa		gatgctgcca cttattactg ccaacagtgg	1440
agtagtaacc cgctcacgtt cggtggcggg		accaaggtgg agatcaaa	1488

<210> 237

<211> 496

<212> PRT

<213> artificial sequence

<220>

<223> 5-10xVH5VL1 LHHL

<400> 237

Glu Leu Val Met Thr Gln Ser Pro Ser Ser Leu Thr Val Thr Ala Gly
1 5 10 15

Glu Lys Val Thr Met Ser Cys Lys Ser Ser Gln Ser Leu Leu Asn Ser
20 25 30

Gly Asn Gln Lys Asn Tyr Leu Thr Trp Tyr Gln Gln Lys Pro Gly Gln
35 40 45

Pro Pro Lys Leu Leu Ile Tyr Trp Ala Ser Thr Arg Glu Ser Gly Val
50 55 60

Pro Asp Arg Phe Thr Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
65 70 75 80

Ile Ser Ser Val Gln Ala Glu Asp Leu Ala Val Tyr Tyr Cys Gln Asn
85 90 95

Asp Tyr Ser Tyr Pro Leu Thr Phe Gly Ala Gly Thr Lys Leu Glu Ile
100 105 110

Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
115 120 125

Glu Val Gln Leu Leu Glu Gln Ser Gly Ala Glu Leu Val Arg Pro Gly
130 135 140

Thr Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Thr Asn
145 150 155 160

Tyr Trp Leu Gly Trp Val Lys Gln Arg Pro Gly His Gly Leu Glu Trp
165 170 175

Ile Gly Asp Ile Phe Pro Gly Ser Gly Asn Ile His Tyr Asn Glu Lys
180 185 190

Phe Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala
 195 200 205
 Tyr Met Gln Leu Ser Ser Leu Thr Phe Glu Asp Ser Ala Val Tyr Phe
 210 215 220
 Cys Ala Arg Leu Arg Asn Trp Asp Glu Pro Met Asp Tyr Trp Gly Gln
 225 230 235 240
 Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp Val Gln
 245 250 255
 Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys
 260 265 270
 Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His
 275 280 285
 Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile
 290 295 300
 Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val Lys Gly Arg
 305 310 315 320
 Phe Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu
 325 330 335
 Ser Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys Ala Arg Tyr
 340 345 350
 Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val
 355 360 365
 Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly Gly Ser Gly
 370 375 380
 Gly Ser Gly Gly Ala Asp Asp Ile Gln Met Thr Gln Ser Pro Ser Ser
 385 390 395 400
 Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser
 405 410 415
 Gln Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala
 420 425 430
 Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser Gly Val Pro
 435 440 445
 Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile
 450 455 460

Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp
 465 470 475 480

Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
 485 490 495

<210> 238

<211> 1491

<212> DNA

<213> artificial sequence

<220>

<223> 5-10xVH5VL1 HLHL

<400> 238
 gaggtgcagc tgctcgagca gtctggagct gagctggtaa ggcctgggac ttcagtgaag 60
 atatcctgca aggcttctgg atacgccttc actaactact ggctagggttg ggtaaagcag 120
 aggcctggac atggacttga gtggattgga gatattttcc ctggaagtgg taatatccac 180
 tacaatgaga agttcaaggg caaagccaca ctgactgcag acaaactcttc gagcacagcc 240
 tatatgcagc tcagtagcct gacatttgag gactctgctg tctattttctg tgcaagactg 300
 aggaactggg acgagcctat ggactactgg ggccaagggg ccacggtcac cgtctcctca 360
 ggtggtggtg gttctggcgg cggcggctcc ggtggtggtg gttctgagct cgtgatgaca 420
 cagtctccat cctccctgac tgtgacagca ggagagaagg tcactatgag ctgcaagtcc 480
 agtcagagtc tgttaaacag tggaaatcaa aagaactact tgacctggta ccagcagaaa 540
 ccagggcagc ctctaaact gttgatctac tgggcatcca ctagggaatc tgggggtccct 600
 gatcgcttca caggcagtgg atctggaaca gatttcactc tcaccatcag cagtgtgcag 660
 gctgaagacc tggcagttta ttactgtcag aatgattata gttatccgct cacgttcggt 720
 gctgggacca agcttgagat caaatccgga ggtggtggat ccgacgtcca actggtgcag 780
 tcaggggctg aagtgaaaaa acctggggcc tcagtgaagg tgtcctgcaa ggcttctggc 840
 tacaccttta ctaggtacac gatgcactgg gtaaggcagg cacctggaca gggctctggaa 900
 tggattggat acattaatcc tagccgtggg tataactaatt acgcagacag cgtcaagggc 960
 cgcttcacaa tcactacaga caaatccacc agcacagcct acatggaact gagcagcctg 1020
 cgttctgagg aactgcaac ctattactgt gcaagatatt atgatgatca ttactgcctt 1080
 gactactggg gccaaggcac cacggtcacc gtctcctcag gcgaaggtag tagtactggt 1140
 tctggtggaa gtggagggtc aggtggagca gacgacattc agatgacca gtctccatct 1200
 agcctgtctg catctgtcgg ggaccgtgtc accatcacct gcagagccag tcaaagtgtg 1260
 agttacatga actggtacca gcagaagccg ggcaaggcac ccaaagatg gatttatgac 1320
 acatccaaag tggcttctgg agtccttgct cgcttcagtg gcagtgggtc tgggaccgac 1380

tactctctca caatcaacag cttggaggct gaagatgctg ccacttatta ctgccaacag 1440
 tggagtagta acccgctcac gttcggtggc gggaccaagg tggagatcaa a 1491

<210> 239

<211> 497

<212> PRT

<213> artificial sequence

<220>

<223> 5-10xVH5VL1 HLHL

<400> 239

Glu Val Gln Leu Leu Glu Gln Ser Gly Ala Glu Leu Val Arg Pro Gly
 1 5 10 15

Thr Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Thr Asn
 20 25 30

Tyr Trp Leu Gly Trp Val Lys Gln Arg Pro Gly His Gly Leu Glu Trp
 35 40 45

Ile Gly Asp Ile Phe Pro Gly Ser Gly Asn Ile His Tyr Asn Glu Lys
 50 55 60

Phe Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala
 65 70 75 80

Tyr Met Gln Leu Ser Ser Leu Thr Phe Glu Asp Ser Ala Val Tyr Phe
 85 90 95

Cys Ala Arg Leu Arg Asn Trp Asp Glu Pro Met Asp Tyr Trp Gly Gln
 100 105 110

Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly
 115 120 125

Gly Ser Gly Gly Gly Gly Ser Glu Leu Val Met Thr Gln Ser Pro Ser
 130 135 140

Ser Leu Thr Val Thr Ala Gly Glu Lys Val Thr Met Ser Cys Lys Ser
 145 150 155 160

Ser Gln Ser Leu Leu Asn Ser Gly Asn Gln Lys Asn Tyr Leu Thr Trp
 165 170 175

Tyr Gln Gln Lys Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr Trp Ala
 180 185 190

Ser Thr Arg Glu Ser Gly Val Pro Asp Arg Phe Thr Gly Ser Gly Ser
195 200 205

Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Val Gln Ala Glu Asp Leu
210 215 220

Ala Val Tyr Tyr Cys Gln Asn Asp Tyr Ser Tyr Pro Leu Thr Phe Gly
225 230 235 240

Ala Gly Thr Lys Leu Glu Ile Lys Ser Gly Gly Gly Gly Ser Asp Val
245 250 255

Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val
260 265 270

Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met
275 280 285

His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr
290 295 300

Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val Lys Gly
305 310 315 320

Arg Phe Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu
325 330 335

Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys Ala Arg
340 345 350

Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr
355 360 365

Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly Gly Ser
370 375 380

Gly Gly Ser Gly Gly Ala Asp Asp Ile Gln Met Thr Gln Ser Pro Ser
385 390 395 400

Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala
405 410 415

Ser Gln Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro Gly Lys
420 425 430

Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser Gly Val
435 440 445

Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr
450 455 460

Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys Gln Gln
 465 470 475 480

Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile
 485 490 495

Lys

<210> 240

<211> 1488

<212> DNA

<213> artificial sequence

<220>

<223> 5-10xVL1VH5 LHLH

<400> 240

gagctcgtga	tgacacagtc	tccatcctcc	ctgactgtga	cagcaggaga	gaaggtcact	60
atgagctgca	agtccagtc	gagtctgtta	aacagtggaa	atcaaaagaa	ctacttgacc	120
tggtaccagc	agaaaccagg	gcagcctcct	aaactgttga	tctactgggc	atccactagg	180
gaatctgggg	tccctgatcg	cttcacaggc	agtggatctg	gaacagattt	cactctcacc	240
atcagcagtg	tgaggctga	agacctggca	gtttattact	gtcagaatga	ttatagttat	300
ccgctcacgt	tcggtgctgg	gaccaagctt	gagatcaaag	gtggtggtgg	ttctggcggc	360
ggcggctccg	gtggtggtgg	ttctgaggtg	cagctgctcg	agcagtctgg	agctgagctg	420
gtaaggcctg	ggacttcagt	gaagatatcc	tgcaaggctt	ctggatacgc	cttcactaac	480
tactggctag	gttgggtaaa	gcagaggcct	ggacatggac	ttgagtggat	tggagatatt	540
ttccctggaa	gtggtaatat	ccactacaat	gagaagttca	agggcaaagc	cacactgact	600
gcagacaaat	cttcgagcac	agcctatatg	cagctcagta	gcctgacatt	tgaggactct	660
gctgtctatt	tctgtgcaag	actgaggaac	tgggacgagc	ctatggacta	ctggggccaa	720
gggaccacgg	tcaccgtctc	ctccggagg	ggtggatccg	acattcagat	gaccagctct	780
ccatctagcc	tgtctgcatc	tgtcggggac	cgtgtcacca	tcacctgcag	agccagtcaa	840
agtgtgaagt	acatgaactg	gtaccagcag	aagccgggca	aggcacccaa	aagatggatt	900
tatgacacat	ccaaagtggc	ttctggagtc	cctgctcgct	tcagtggcag	tgggtctggg	960
accgactact	ctctcacaat	caacagcttg	gaggctgaag	atgctgccac	ttattactgc	1020
caacagtgga	gtagtaaccc	gctcacgttc	ggtggcggga	ccaagggtga	gatcaaaggc	1080
gaaggtaact	gtactgggtc	tggtggaagt	ggaggttcag	gtggagcaga	cgacgtccaa	1140
ctggtgcagt	caggggctga	agtgaaaaaa	cctggggcct	cagtgaagg	gtcctgcaag	1200
gcttctggct	acacctttac	taggtacacg	atgcactggg	taaggcaggc	acctggacag	1260

ggtctggaat ggattggata cattaatcct agccgtgggtt atactaatta cgcagacagc 1320
 gtcaagggcc gcttcacaat cactacagac aaatccacca gcacagccta catggaactg 1380
 agcagcctgc gttctgagga cactgcaacc tattactgtg caagatatta tgatgatcat 1440
 tactgccttg actactgggg ccaaggcacc acggtcaccg tctcctca 1488

<210> 241

<211> 496

<212> PRT

<213> artificial sequence

<220>

<223> 5-10xVL1VH5 LHLH

<400> 241

Glu Leu Val Met Thr Gln Ser Pro Ser Ser Leu Thr Val Thr Ala Gly
 1 5 10 15

Glu Lys Val Thr Met Ser Cys Lys Ser Ser Gln Ser Leu Leu Asn Ser
 20 25 30

Gly Asn Gln Lys Asn Tyr Leu Thr Trp Tyr Gln Gln Lys Pro Gly Gln
 35 40 45

Pro Pro Lys Leu Leu Ile Tyr Trp Ala Ser Thr Arg Glu Ser Gly Val
 50 55 60

Pro Asp Arg Phe Thr Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
 65 70 75 80

Ile Ser Ser Val Gln Ala Glu Asp Leu Ala Val Tyr Tyr Cys Gln Asn
 85 90 95

Asp Tyr Ser Tyr Pro Leu Thr Phe Gly Ala Gly Thr Lys Leu Glu Ile
 100 105 110

Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Ser
 115 120 125

Glu Val Gln Leu Leu Glu Gln Ser Gly Ala Glu Leu Val Arg Pro Gly
 130 135 140

Thr Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Thr Asn
 145 150 155 160

Tyr Trp Leu Gly Trp Val Lys Gln Arg Pro Gly His Gly Leu Glu Trp
 165 170 175

Ile Gly Asp Ile Phe Pro Gly Ser Gly¹⁸⁵ Asn¹⁹⁷ Ile His Tyr Asn¹⁹⁰ Glu Lys
 Phe Lys Gly¹⁹⁵ Lys Ala Thr Leu Thr²⁰⁰ Ala Asp Lys Ser Ser²⁰⁵ Ser Thr Ala
 Tyr Met²¹⁰ Gln Leu Ser Ser²¹⁵ Leu Thr Phe Glu Asp Ser²²⁰ Ala Val Tyr Phe
 Cys²²⁵ Ala Arg Leu Arg Asn²³⁰ Trp Asp Glu Pro Met²³⁵ Asp Tyr Trp Gly Gln²⁴⁰
 Gly Thr Thr Val Thr²⁴⁵ Val Ser Ser Gly Gly²⁵⁰ Gly Gly Ser Asp Ile²⁵⁵ Gln
 Met Thr Gln Ser²⁶⁰ Pro Ser Ser²⁶⁵ Leu Ser Ala Ser Val Gly Asp Arg Val²⁷⁰
 Thr Ile Thr²⁷⁵ Cys Arg Ala Ser Gln²⁸⁰ Ser Val Ser Tyr Met²⁸⁵ Asn Trp Tyr
 Gln Gln²⁹⁰ Lys Pro Gly Lys Ala²⁹⁵ Pro Lys Arg Trp Ile³⁰⁰ Tyr Asp Thr Ser
 Lys³⁰⁵ Val Ala Ser Gly Val³¹⁰ Pro Ala Arg Phe Ser³¹⁵ Gly Ser Gly Ser Gly³²⁰
 Thr Asp Tyr Ser³²⁵ Leu Thr Ile Asn Ser³³⁰ Leu Glu Ala Glu Asp Ala³³⁵ Ala
 Thr Tyr Tyr Cys³⁴⁰ Gln Gln Trp Ser Ser³⁴⁵ Asn Pro Leu Thr Phe³⁵⁰ Gly Gly
 Gly Thr Lys³⁵⁵ Val Glu Ile Lys Gly³⁶⁰ Glu Gly Thr Ser Thr³⁶⁵ Gly Ser Gly
 Gly Ser³⁷⁰ Gly Gly Ser Gly³⁷⁵ Ala Asp Asp Val Gln³⁸⁰ Leu Val Gln Ser
 Gly³⁸⁵ Ala Glu Val Lys Lys³⁹⁰ Pro Gly Ala Ser Val³⁹⁵ Lys Val Ser Cys Lys⁴⁰⁰
 Ala Ser Gly Tyr Thr⁴⁰⁵ Phe Thr Arg Tyr Thr⁴¹⁰ Met His Trp Val Arg⁴¹⁵ Gln
 Ala Pro Gly Gln⁴²⁰ Gly Leu Glu Trp Ile⁴²⁵ Gly Tyr Ile Asn Pro Ser Arg⁴³⁰
 Gly Tyr Thr⁴³⁵ Asn Tyr Ala Asp Ser⁴⁴⁰ Val Lys Gly Arg Phe⁴⁴⁵ Thr Ile Thr
 Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg

450 455 198 460
 Ser Glu Asp Thr Ala Thr Tyr Tyr Cys Ala Arg Tyr Tyr Asp Asp His
 465 470 475 480
 Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
 485 490 495

<210> 242
 <211> 1491
 <212> DNA
 <213> artificial sequence

<220>

<223> 5-10xVL1VH5 HLLH

<400> 242
 gaggtgcagc tgctcgagca gtctggagct gagctggtaa ggcctgggac ttcagtgaag 60
 atatcctgca aggcttctgg atacgccttc actaactact ggctagggttg ggtaaagcag 120
 aggcctggac atggacttga gtggattgga gatattttcc ctggaagtgg taatatccac 180
 tacaatgaga agttcaaggg caaagccaca ctgactgcag acaaattcttc gagcacagcc 240
 tatatgcagc tcagtagcct gacatttgag gactctgctg tctattttctg tgcaagactg 300
 aggaactggg acgagcctat ggactactgg ggccaagggg ccacgggtcac cgtctcctca 360
 ggtggtggtg gttctggcgg cggcggctcc ggtggtggtg gttctgagct cgtgatgaca 420
 cagtctccat cctccctgac tgtgacagca ggagagaagg tcactatgag ctgcaagtcc 480
 agtcagagtc tgttaaacag tggaaatcaa aagaactact tgacctggta ccagcagaaa 540
 ccagggcagc ctcttaaact gttgatctac tgggcatcca ctagggaatc tggggtcctc 600
 gatcgcttca caggcagtgg atctggaaca gatttcactc tcaccatcag cagtgtgcag 660
 gctgaagacc tggcagttta ttactgtcag aatgattata gttatccgct cacgttcggt 720
 gctgggacca agcttgagat caaatccgga ggtggtggat ccgacattca gatgacctag 780
 tctccatcta gcctgtctgc atctgtcggg gaccgtgtca ccatcacctg cagagccagt 840
 caaagtgtaa gttacatgaa ctggtaccag cagaagccgg gcaaggcacc caaaagatgg 900
 atttatgaca catccaaagt ggcttctgga gtccctgctc gcttcagtgg cagtgggtct 960
 gggaccgact actctctcac aatcaacagc ttggaggctg aagatgctgc cacttattac 1020
 tgccaacagt ggagtagtaa cccgctcacg ttcggtggcg ggaccaaggt ggagatcaaa 1080
 ggcgaaggta ctagtactgg ttctggtgga agtggagggt cagggtggagc agacgacgtc 1140
 caactggtgc agtcaggggc tgaagtgaaa aaacctgggg cctcagtga ggtgtcctgc 1200
 aaggcttctg gctacacctt tactaggtac acgatgcact gggtaaggca ggcacctgga 1260
 cagggtctgg aatggattgg atacattaat cctagccgtg gttatactaa ttacgcagac 1320

agcgtcaagg gccgcttcac aatcactaca gacaaatcca ccagcacagc ctacatggaa 1380
 ctgagcagcc tgcgttctga ggacactgca acctattact gtgcaagata ttatgatgat 1440
 cattactgcc ttgactactg gggccaaggc accacgggtca ccgtctcctc a 1491

<210> 243

<211> 497

<212> PRT

<213> artificial sequence

<220>

<223> 5-10xVL1VH5 HLLH

<400> 243

Glu Val Gln Leu Leu Glu Gln Ser Gly Ala Glu Leu Val Arg Pro Gly
 1 5 10 15

Thr Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Thr Asn
 20 25 30

Tyr Trp Leu Gly Trp Val Lys Gln Arg Pro Gly His Gly Leu Glu Trp
 35 40 45

Ile Gly Asp Ile Phe Pro Gly Ser Gly Asn Ile His Tyr Asn Glu Lys
 50 55 60

Phe Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala
 65 70 75 80

Tyr Met Gln Leu Ser Ser Leu Thr Phe Glu Asp Ser Ala Val Tyr Phe
 85 90 95

Cys Ala Arg Leu Arg Asn Trp Asp Glu Pro Met Asp Tyr Trp Gly Gln
 100 105 110

Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly
 115 120 125

Gly Ser Gly Gly Gly Gly Ser Glu Leu Val Met Thr Gln Ser Pro Ser
 130 135 140

Ser Leu Thr Val Thr Ala Gly Glu Lys Val Thr Met Ser Cys Lys Ser
 145 150 155 160

Ser Gln Ser Leu Leu Asn Ser Gly Asn Gln Lys Asn Tyr Leu Thr Trp
 165 170 175

Tyr Gln Gln Lys Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr Trp Ala

				180					185		200				190		
Ser	Thr	Arg	Glu	Ser	Gly	Val	Pro	Asp	Arg	Phe	Thr	Gly	Ser	Gly	Ser		
		195					200					205					
Gly	Thr	Asp	Phe	Thr	Leu	Thr	Ile	Ser	Ser	Val	Gln	Ala	Glu	Asp	Leu		
	210					215					220						
Ala	Val	Tyr	Tyr	Cys	Gln	Asn	Asp	Tyr	Ser	Tyr	Pro	Leu	Thr	Phe	Gly		
225					230					235					240		
Ala	Gly	Thr	Lys	Leu	Glu	Ile	Lys	Ser	Gly	Gly	Gly	Gly	Ser	Asp	Ile		
				245					250					255			
Gln	Met	Thr	Gln	Ser	Pro	Ser	Ser	Leu	Ser	Ala	Ser	Val	Gly	Asp	Arg		
			260					265					270				
Val	Thr	Ile	Thr	Cys	Arg	Ala	Ser	Gln	Ser	Val	Ser	Tyr	Met	Asn	Trp		
		275					280					285					
Tyr	Gln	Gln	Lys	Pro	Gly	Lys	Ala	Pro	Lys	Arg	Trp	Ile	Tyr	Asp	Thr		
	290					295					300						
Ser	Lys	Val	Ala	Ser	Gly	Val	Pro	Ala	Arg	Phe	Ser	Gly	Ser	Gly	Ser		
305					310					315					320		
Gly	Thr	Asp	Tyr	Ser	Leu	Thr	Ile	Asn	Ser	Leu	Glu	Ala	Glu	Asp	Ala		
				325					330					335			
Ala	Thr	Tyr	Tyr	Cys	Gln	Gln	Trp	Ser	Ser	Asn	Pro	Leu	Thr	Phe	Gly		
			340					345					350				
Gly	Gly	Thr	Lys	Val	Glu	Ile	Lys	Gly	Glu	Gly	Thr	Ser	Thr	Gly	Ser		
		355					360					365					
Gly	Gly	Ser	Gly	Gly	Ser	Gly	Gly	Ala	Asp	Asp	Val	Gln	Leu	Val	Gln		
	370					375					380						
Ser	Gly	Ala	Glu	Val	Lys	Lys	Pro	Gly	Ala	Ser	Val	Lys	Val	Ser	Cys		
385					390					395					400		
Lys	Ala	Ser	Gly	Tyr	Thr	Phe	Thr	Arg	Tyr	Thr	Met	His	Trp	Val	Arg		
				405					410					415			
Gln	Ala	Pro	Gly	Gln	Gly	Leu	Glu	Trp	Ile	Gly	Tyr	Ile	Asn	Pro	Ser		
			420					425					430				
Arg	Gly	Tyr	Thr	Asn	Tyr	Ala	Asp	Ser	Val	Lys	Gly	Arg	Phe	Thr	Ile		
		435					440					445					
Thr	Thr	Asp	Lys	Ser	Thr	Ser	Thr	Ala	Tyr	Met	Glu	Leu	Ser	Ser	Leu		
	450					455					460						

Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys Ala Arg Tyr Tyr Asp Asp
 465 470 475 480

His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser
 485 490 495

Ser

<210> 244

<211> 1491

<212> DNA

<213> artificial sequence

<220>

<223> 5-10xVH5VL2 HLHL

<400> 244

gaggtgcagc tgctcgagca gtctggagct gagctggtaa ggcctgggac ttcagtgaag	60
atatacctgca aggcttctgg atacgccttc actaactact ggctagggtg ggtaaagcag	120
aggcctggac atggacttga gtggattgga gatattttcc ctggaagtgg taatatccac	180
tacaatgaga agttcaaggg caaagccaca ctgactgcag acaaatcttc gagcacagcc	240
tatatgcagc tcagtagcct gacatttgag gactctgctg tctatttctg tgcaagactg	300
aggaactggg acgagcctat ggactactgg ggccaaggga ccacggtcac cgtctcctca	360
ggtggtggtg gttctggcgg cggcggctcc ggtggtggtg gttctgagct cgtgatgaca	420
cagtctccat cctccctgac tgtgacagca ggagagaagg tcactatgag ctgcaagtcc	480
agtcagagtc tgtaaacag tggaaatcaa aagaactact tgacctggta ccagcagaaa	540
ccagggcagc ctccataaact gttgatctac tgggcatcca ctagggaatc tgggggtccct	600
gatcgcttca caggcagtgg atctggaaca gatttcactc tcaccatcag cagtgtgcag	660
gctgaagacc tggcagttta ttactgtcag aatgattata gttatccgct cacgttcggt	720
gctgggacca agcttgagat caaatccgga ggtggtggat ccgacgtcca actggtgcag	780
tcaggggctg aagtgaaaaa acctggggcc tcagtgaagg tgcctgcaa ggcttctggc	840
tacaccttta ctaggtacac gatgcactgg gtaaggcagg cacctggaca gggctctggaa	900
tggattggat acattaatcc tagccgtggt tataactaatt acgcagacag cgtcaagggc	960
cgcttcacaa tcactacaga caaatccacc agcacagcct acatggaact gagcagcctg	1020
cgttctgagg aactgcaac ctattactgt gcaagatatt atgatgatca ttactgcctt	1080
gactactggg gccaaggcac cacggtcacc gtctcctcag gcgaaggtag tagtactggt	1140
tctggtggaa gtggagggttc aggtggagca gacgacattg tactgacca gtctccagca	1200

202

actctgtctc tgtctccagg ggagcgtgcc accctgagct gcagagccag tcaaagtgtgta	1260
agttacatga actggtacca gcagaagccg ggcaaggcac ccaaaagatg gatttatgac	1320
acatccaaag tggcttctgg agtccctgct cgcttcagtgc gcagtgggtc tgggaccgac	1380
tactctctca caatcaacag cttggaggct gaagatgctg ccacttatta ctgccaacag	1440
tggagtagta acccgctcac gttcggtggc gggaccaagg tggagatcaa a	1491

<210> 245

<211> 497

<212> PRT

<213> artificial sequence

<220>

<223> 5-10xVH5VL2 HLHL

<400> 245

Glu Val Gln Leu Leu Glu Gln Ser Gly Ala Glu Leu Val Arg Pro Gly
1 5 10 15

Thr Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Thr Asn
20 25 30

Tyr Trp Leu Gly Trp Val Lys Gln Arg Pro Gly His Gly Leu Glu Trp
35 40 45

Ile Gly Asp Ile Phe Pro Gly Ser Gly Asn Ile His Tyr Asn Glu Lys
50 55 60

Phe Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala
65 70 75 80

Tyr Met Gln Leu Ser Ser Leu Thr Phe Glu Asp Ser Ala Val Tyr Phe
85 90 95

Cys Ala Arg Leu Arg Asn Trp Asp Glu Pro Met Asp Tyr Trp Gly Gln
100 105 110

Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly
115 120 125

Gly Ser Gly Gly Gly Gly Ser Glu Leu Val Met Thr Gln Ser Pro Ser
130 135 140

Ser Leu Thr Val Thr Ala Gly Glu Lys Val Thr Met Ser Cys Lys Ser
145 150 155 160

Ser Gln Ser Leu Leu Asn Ser Gly Asn Gln Lys Asn Tyr Leu Thr Trp
165 170 175

Tyr Gln Gln Lys Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr Trp Ala
 180 185 190
 Ser Thr Arg Glu Ser Gly Val Pro Asp Arg Phe Thr Gly Ser Gly Ser
 195 200 205
 Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Val Gln Ala Glu Asp Leu
 210 215 220
 Ala Val Tyr Tyr Cys Gln Asn Asp Tyr Ser Tyr Pro Leu Thr Phe Gly
 225 230 235 240
 Ala Gly Thr Lys Leu Glu Ile Lys Ser Gly Gly Gly Gly Ser Asp Val
 245 250 255
 Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val
 260 265 270
 Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met
 275 280 285
 His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr
 290 295 300
 Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val Lys Gly
 305 310 315 320
 Arg Phe Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu
 325 330 335
 Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys Ala Arg
 340 345 350
 Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr
 355 360 365
 Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly Gly Ser
 370 375 380
 Gly Gly Ser Gly Gly Ala Asp Asp Ile Val Leu Thr Gln Ser Pro Ala
 385 390 395 400
 Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala
 405 410 415
 Ser Gln Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro Gly Lys
 420 425 430
 Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser Gly Val
 435 440 445

Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr
 450 455 460

Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys Gln Gln
 465 470 475 480

Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile
 485 490 495

Lys

<210> 246

<211> 1488

<212> DNA

<213> artificial sequence

<220>

<223> 5-10xVL2VH5 LHLH

<400> 246

gagctcgtga tgacacagtc tccatcctcc ctgactgtga cagcaggaga gaaggtcact	60
atgagctgca agtccagtca gagtctgtta aacagtggaa atcaaaagaa ctacttgacc	120
tggtaccagc agaaaccagg gcagcctcct aaactgttga tctactgggc atccactagg	180
gaatctgggg tccctgatcg cttcacaggc agtggatctg gaacagattt cactctcacc	240
atcagcagtg tgcaggctga agacctggca gtttattact gtcagaatga ttatagttat	300
ccgctcacgt tcggtgctgg gaccaagctt gagatcaaag gtggtggtgg ttctggcggc	360
ggcggctccg gtggtggtgg ttctgaggtg cagctgctcg agcagtctgg agctgagctg	420
gtaaggcctg ggacttcagt gaagatatcc tgcaaggctt ctggatacgc cttcactaac	480
tactggctag gttgggtaaa gcagaggcct ggacatggac ttgagtggat tggagatatt	540
ttccctggaa gtggtaatat ccactacaat gagaagttca agggcaaagc cactctgact	600
gcagacaaat cttcgagcac agcctatatg cagctcagta gcctgacatt tgaggactct	660
gctgtctatt tctgtgcaag actgaggaac tgggacgagc ctatggacta ctggggccaa	720
gggaccacgg tcaccgtctc ctccggaggt ggtggatccg acattgtact gacccagtct	780
ccagcaactc tgtctctgtc tccaggggag cgtgccaccc tgagctgcag agccagtcaa	840
agtgtgaagt acatgaactg gtaccagcag aagccgggca aggcacccaa aagatggatt	900
tatgacacat ccaaagtggc ttctggagtc cctgctcgct tcagtggcag tgggtctggg	960
accgactact ctctcacaat caacagcttg gaggtgaag atgctgccac ttattactgc	1020
caacagtgga gtagtaacct gctcacgttc ggtggcggga ccaaggtgga gatcaaaggc	1080
gaaggacta gtactggttc tggtggaagt ggaggttcag gtggagcaga cgacgtccaa	1140

ctggtgcagt caggggctga agtgaaaaaa cctggggcct cagtgaaggt gtcctgcaag 1200
gcttctggct acacctttac taggtacacg atgcactggg taaggcaggc acctggacag 1260
ggctctggaat ggattggata cattaatcct agccgtgggt atactaatta cgcagacagc 1320
gtcaagggcc gcttcacaat cactacagac aaatccacca gcacagccta catggaactg 1380
agcagcctgc gttctgagga cactgcaacc tattactgtg caagatatta tgatgatcat 1440
tactgccttg actactgggg ccaaggcacc acggtcaccg tctcctca 1488

<210> 247

<211> 496

<212> PRT

<213> artificial sequence

<220>

<223> 5-10xVL2VH5 LHLH

<400> 247

Glu Leu Val Met Thr Gln Ser Pro Ser Ser Leu Thr Val Thr Ala Gly
1 5 10 15

Glu Lys Val Thr Met Ser Cys Lys Ser Ser Gln Ser Leu Leu Asn Ser
20 25 30

Gly Asn Gln Lys Asn Tyr Leu Thr Trp Tyr Gln Gln Lys Pro Gly Gln
35 40 45

Pro Pro Lys Leu Leu Ile Tyr Trp Ala Ser Thr Arg Glu Ser Gly Val
50 55 60

Pro Asp Arg Phe Thr Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
65 70 75 80

Ile Ser Ser Val Gln Ala Glu Asp Leu Ala Val Tyr Tyr Cys Gln Asn
85 90 95

Asp Tyr Ser Tyr Pro Leu Thr Phe Gly Ala Gly Thr Lys Leu Glu Ile
100 105 110

Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
115 120 125

Glu Val Gln Leu Leu Glu Gln Ser Gly Ala Glu Leu Val Arg Pro Gly
130 135 140

Thr Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Thr Asn
145 150 155 160

Tyr Trp Leu Gly Trp Val Lys Gln Arg Pro Gly His Gly Leu Glu Trp
 165 170 175

Ile Gly Asp Ile Phe Pro Gly Ser Gly Asn Ile His Tyr Asn Glu Lys
 180 185 190

Phe Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala
 195 200 205

Tyr Met Gln Leu Ser Ser Leu Thr Phe Glu Asp Ser Ala Val Tyr Phe
 210 215 220

Cys Ala Arg Leu Arg Asn Trp Asp Glu Pro Met Asp Tyr Trp Gly Gln
 225 230 235 240

Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp Ile Val
 245 250 255

Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala
 260 265 270

Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Tyr Met Asn Trp Tyr
 275 280 285

Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser
 290 295 300

Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly
 305 310 315 320

Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala
 325 330 335

Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly
 340 345 350

Gly Thr Lys Val Glu Ile Lys Gly Glu Gly Thr Ser Thr Gly Ser Gly
 355 360 365

Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Val Gln Leu Val Gln Ser
 370 375 380

Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys
 385 390 395 400

Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp Val Arg Gln
 405 410 415

Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn Pro Ser Arg
 420 425 430

Gly Tyr Thr Asn Tyr Ala Asp Ser Val Lys²⁰⁷ Gly Arg Phe Thr Ile Thr
 435 440 445

Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg
 450 455 460

Ser Glu Asp Thr Ala Thr Tyr Tyr Cys Ala Arg Tyr Tyr Asp Asp His
 465 470 475 480

Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
 485 490 495

<210> 248

<211> 1491

<212> DNA

<213> artificial sequence

<220>

<223> 5-10xVL2VH5 HLLH

<400> 248

gaggtgcagc	tgctcgagca	gtctggagct	gagctggtaa	ggcctgggac	ttcagtgaag	60
atatcctgca	aggcttctgg	atacgcttc	actaactact	ggctagggttg	ggtaaagcag	120
aggcctggac	atggacttga	gtggattgga	gatattttcc	ctggaagtgg	taatatccac	180
tacaatgaga	agttcaaggg	caaagccaca	ctgactgcag	acaaatcttc	gagcacagcc	240
tatatgcagc	tcagtagcct	gacatttgag	gactctgctg	tctatttctg	tgcaagactg	300
aggaactggg	acgagcctat	ggactactgg	ggccaaggga	ccacggtcac	cgtctcctca	360
ggtggtggtg	gttctggcgg	cggcggctcc	ggtggtggtg	gttctgagct	cgtgatgaca	420
cagtctccat	cctccctgac	tgtgacagca	ggagagaagg	tcactatgag	ctgcaagtcc	480
agtcagagtc	tgttaaacag	tggaatatcaa	aagaactact	tgacctggta	ccagcagaaa	540
ccagggcagc	ctcctaaact	gttgatctac	tgggcatcca	ctaggggaatc	tgggggtccct	600
gatcgcttca	caggcagtgg	atctggaaca	gatttcactc	tcaccatcag	cagtgtgcag	660
gctgaagacc	tggcagttta	ttactgtcag	aatgattata	gttatccgct	cacgttcggt	720
gctgggacca	agcttgagat	caaatccgga	ggtggtggat	ccgacattgt	actgacccag	780
tctccagcaa	ctctgtctct	gtctccaggg	gagcgtgccca	ccctgagctg	cagagccagt	840
caaagtgtaa	gttacetgaa	ctgggtaccag	cagaagccgg	gcaaggcacc	caaaagatgg	900
atztatgaca	catccaaagt	ggcttctgga	gtccctgctc	gcttcagtgg	cagtgggtct	960
gggaccgact	actctctcac	aatcaacagc	ttggaggctg	aagatgctgc	cacttattac	1020
tgccaacagt	ggagtagtaa	cccgcctcacg	ttcgggtggcg	ggaccaagggt	ggagatcaaa	1080
ggcgaaggta	ctagtactgg	ttctgggtgga	agtggagggtt	caggtggagc	agacgacgtc	1140

208

caactggtgc agtcaggggc tgaagtgaaa aaacctgggg cctcagtgaa ggtgtcctgc	1200
aaggcttctg gctacacctt tactaggtac acgatgcact gggtaaggca ggcacctgga	1260
cagggctctgg aatggattgg atacattaat cctagccgtg gttatactaa ttacgcagac	1320
agcgtcaagg gccgcttcac aatcactaca gacaaatcca ccagcacagc ctacatggaa	1380
ctgagcagcc tgcgttctga ggacactgca acctattact gtgcaagata ttatgatgat	1440
cattactgcc ttgactactg gggccaaggc accacggtca cgtctctc a	1491

<210> 249

<211> 497

<212> PRT

<213> artificial sequence

<220>

<223> 5-10xVL2VH5 HLLH

<400> 249

Glu Val Gln Leu ⁵ Leu Glu Gln Ser Gly Ala Glu Leu Val Arg Pro Gly
1 10 15

Thr Ser Val Lys ²⁰ Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Thr Asn
25 30

Tyr Trp Leu Gly Trp Val Lys ⁴⁰ Gln Arg Pro Gly His Gly Leu Glu Trp
35 45

Ile Gly Asp Ile Phe Pro Gly ⁵⁵ Ser Gly Asn Ile His Tyr Asn Glu Lys
50 60

Phe Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys ⁷⁵ Ser Ser Ser Thr Ala
65 70 80

Tyr Met Gln Leu Ser ⁸⁵ Ser Leu Thr Phe Glu Asp Ser Ala Val Tyr Phe
90 95

Cys Ala Arg Leu Arg Asn Trp Asp Glu ¹⁰⁵ Pro Met Asp Tyr Trp Gly Gln
100 110

Gly Thr Thr Val Thr Val Ser ¹²⁰ Ser Gly Gly Gly Gly Ser Gly Gly Gly
115 125

Gly ser Gly Gly Gly Gly ¹³⁵ Ser Glu Leu Val Met Thr Gln Ser Pro Ser
130 140

Ser Leu Thr Val Thr Ala ¹⁵⁰ Gly Glu Lys Val Thr Met Ser Cys Lys Ser
145 155 160

Ser Gln Ser Leu Leu Asn Ser Gly Asn Gln²⁰⁹ Lys Asn Tyr Leu Thr Trp
 165 170 175
 Tyr Gln Gln Lys Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr Trp Ala
 180 185 190
 Ser Thr Arg Glu Ser Gly Val Pro Asp Arg Phe Thr Gly Ser Gly Ser
 195 200 205
 Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Val Gln Ala Glu Asp Leu
 210 215 220
 Ala Val Tyr Tyr Cys Gln Asn Asp Tyr Ser Tyr Pro Leu Thr Phe Gly
 225 230 235 240
 Ala Gly Thr Lys Leu Glu Ile Lys Ser Gly Gly Gly Gly Ser Asp Ile
 245 250 255
 Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg
 260 265 270
 Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Tyr Met Asn Trp
 275 280 285
 Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr
 290 295 300
 Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser
 305 310 315 320
 Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala
 325 330 335
 Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly
 340 345 350
 Gly Gly Thr Lys Val Glu Ile Lys Gly Glu Gly Thr Ser Thr Gly Ser
 355 360 365
 Gly Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Val Gln Leu Val Gln
 370 375 380
 Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys
 385 390 395 400
 Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp Val Arg
 405 410 415
 Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn Pro Ser
 420 425 430
 Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile

tactggggcc aaggcaccac ggtcaccgtc tcctcaggcg aaggtactag tactggttct 1140
 ggtggaagtg gaggttcagg tggagcagac gacattgtac tgacccagtc tccagcaact 1200
 ctgtctctgt ctccagggga gcgtgccacc ctgacctgca gagccagttc aagtgttaagt 1260
 tacatgaact ggtaccagca gaagccgggc aaggcaccca aaagatggat ttatgacaca 1320
 tccaaagtgg cttctggagt ccctgctcgc ttcagtggca gtgggtctgg gaccgactac 1380
 tctctcaciaa tcaacagctt ggaggctgaa gatgctgcca cttattactg ccaacagtgg 1440
 agtagtaacc cgctcacgtt cgggtggcggg accaaggtgg agatcaaa 1488

<210> 251

<211> 496

<212> PRT

<213> artificial sequence

<220>

<223> 5-10VH5VL3 LHHL

<400> 251

Glu Leu Val Met Thr Gln Ser Pro Ser Ser Leu Thr Val Thr Ala Gly
 1 5 10 15

Glu Lys Val Thr Met Ser Cys Lys Ser Ser Gln Ser Leu Leu Asn Ser
 20 25 30

Gly Asn Gln Lys Asn Tyr Leu Thr Trp Tyr Gln Gln Lys Pro Gly Gln
 35 40 45

Pro Pro Lys Leu Leu Ile Tyr Trp Ala Ser Thr Arg Glu Ser Gly Val
 50 55 60

Pro Asp Arg Phe Thr Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
 65 70 75 80

Ile Ser Ser Val Gln Ala Glu Asp Leu Ala Val Tyr Tyr Cys Gln Asn
 85 90 95

Asp Tyr Ser Tyr Pro Leu Thr Phe Gly Ala Gly Thr Lys Leu Glu Ile
 100 105 110

Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
 115 120 125

Glu Val Gln Leu Leu Glu Gln Ser Gly Ala Glu Leu Val Arg Pro Gly
 130 135 140

Thr Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Thr Asn

145	150	212 155	160
Tyr Trp Leu Gly	Trp Val Lys Gln Arg	Pro Gly His Gly Leu	Glu Trp
	165	170	175
Ile Gly Asp	Ile Phe Pro Gly Ser	Gly Asn Ile His Tyr	Asn Glu Lys
	180	185	190
Phe Lys Gly	Lys Ala Thr Leu	Thr Ala Asp Lys Ser	Ser Thr Ala
	195	200	205
Tyr Met Gln Leu Ser Ser	Leu Thr Phe Glu Asp	Ser Ala Val Tyr Phe	
	210	215	220
Cys Ala Arg Leu Arg Asn	Trp Asp Glu Pro Met	Asp Tyr Trp Gly Gln	
	225	230	235
Gly Thr Thr Val	Thr Val Ser Ser Gly	Gly Gly Gly Ser Asp	Val Gln
	245	250	255
Leu Val Gln Ser	Gly Ala Glu Val	Lys Lys Pro Gly Ala	Ser Val Lys
	260	265	270
Val Ser Cys	Lys Ala Ser Gly	Tyr Thr Phe Thr Arg	Tyr Thr Met His
	275	280	285
Trp Val Arg Gln Ala Pro	Gly Gln Gly Leu Glu	Trp Ile Gly Tyr Ile	
	290	295	300
Asn Pro Ser Arg Gly	Tyr Thr Asn Tyr Ala	Asp Ser Val Lys Gly	Arg
	305	310	315
Phe Thr Ile Thr	Thr Asp Lys Ser Thr	Ser Thr Ala Tyr Met	Glu Leu
	325	330	335
Ser Ser Leu Arg	Ser Glu Asp Thr	Ala Thr Tyr Tyr Cys	Ala Arg Tyr
	340	345	350
Tyr Asp Asp	His Tyr Cys Leu	Asp Tyr Trp Gly Gln	Gly Thr Thr Val
	355	360	365

Thr Val Ser Ser Gly Glu	Gly Thr Ser Thr Gly	Ser Gly Gly Ser Gly
	370	375
Gly Ser Gly Gly Ala Asp	Asp Ile Val Leu Thr	Gln Ser Pro Ala Thr
	385	390
Leu Ser Leu Ser Pro Gly Glu Arg Ala	Thr Leu Thr Cys Arg	Ala Ser
	405	410
Ser Ser Val Ser Tyr Met Asn Trp	Tyr Gln Gln Lys Pro	Gly Lys Ala
	420	425
		430

Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser Gly Val Pro
 435 440 445

Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile
 450 455 460

Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp
 465 470 475 480

Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
 485 490 495

<210> 252

<211> 1491

<212> DNA

<213> artificial sequence

<220>

<223> 5-10VH5VL3 HLHL

<400> 252

gaggtgcagc tgctcgagca gtctggagct gagctggtaa ggcctgggac ttcagtgaag	60
atatacctgca aggcttctgg atacgccttc actaactact ggctaggttg ggtaaagcag	120
aggcctggac atggacttga gtggattgga gatattttcc ctggaagtgg taatatccac	180
tacaatgaga agttcaaggg caaagccaca ctgactgcag acaaactctc gagcacagcc	240
tatatgcagc tcagtagcct gacatttgag gactctgctg tctattttctg tgcaagactg	300
aggaactggg acgagcctat ggactactgg ggccaaggga ccacgggtcac cgtctcctca	360
ggtggtggtg gttctggcgg cggcggctcc ggtggtggtg gttctgagct cgtgatgaca	420
cagtctccat cctccctgac tgtgacagca ggagagaagg tcactatgag ctgcaagtcc	480
agtcagagtc tgtaaagcag tggaaatcaa aagaactact tgacctggtg ccagcagaaa	540
ccagggcagc ctctaaact gttgatctac tgggcatcca ctagggaatc tgggggtccct	600
gatcgcttca caggcagtgg atctggaaca gatttcactc tcaccatcag cagtgtgcag	660
gctgaagacc tggcagttta ttactgtcag aatgattata gttatccgct cacgttcggt	720
gctgggacca agcttgagat caaatccgga ggtggtggat ccgacgtcca actggtgcag	780
tcaggggctg aagtgaaaaa acctggggcc tcagtgaagg tgcctgcaa ggcttctggc	840
tacaccttta ctaggtacac gatgcactgg gtaaggcagg cacctggaca gggctctggaa	900
tggattggat acattaatcc tagccgtggt tataactaatt acgcagacag cgtcaagggc	960
cgcttcacaa tcactacaga caaatccacc agcacagcct acatggaact gagcagcctg	1020
cgttctgagg aactgcaac ctattactgt gcaagatatt atgatgatca ttactgcctt	1080

214

gactactggg gccaaaggcac cacgggtcacc gtctcctcag gcgaaggtac tagtactggt	1140
tctggtggaa gtggaggttc aggtggagca gacgacattg tactgaccca gtctccagca	1200
actctgtctc tgtctccagg ggagcgtgcc accctgacct gcagagccag ttcaagtgt	1260
agttacatga actggtacca gcagaagccg ggcaaggcac ccaaaagatg gatttatgac	1320
acatccaaag tggcttctgg agtccctgct cgcttcagtg gcagtgggtc tgggaccgac	1380
tactctctca caatcaacag cttggaggct gaagatgctg ccacttatta ctgccaacag	1440
tggagtagta acccgctcac gttcggtggc gggaccaagg tggagatcaa a	1491

<210> 253

<211> 497

<212> PRT

<213> artificial sequence

<220>

<223> 5-10VH5VL3 HLHL

<400> 253

Glu	Val	Gln	Leu	Leu	Glu	Gln	Ser	Gly	Ala	Glu	Leu	Val	Arg	Pro	Gly
1			5						10					15	

Thr	Ser	Val	Lys	Ile	Ser	Cys	Lys	Ala	Ser	Gly	Tyr	Ala	Phe	Thr	Asn
			20					25					30		

Tyr	Trp	Leu	Gly	Trp	Val	Lys	Gln	Arg	Pro	Gly	His	Gly	Leu	Glu	Trp
		35					40					45			

Ile	Gly	Asp	Ile	Phe	Pro	Gly	Ser	Gly	Asn	Ile	His	Tyr	Asn	Glu	Lys
	50					55					60				

Phe	Lys	Gly	Lys	Ala	Thr	Leu	Thr	Ala	Asp	Lys	Ser	Ser	Ser	Thr	Ala
65					70					75					80

Tyr	Met	Gln	Leu	Ser	Ser	Leu	Thr	Phe	Glu	Asp	Ser	Ala	Val	Tyr	Phe
				85					90					95	

Cys	Ala	Arg	Leu	Arg	Asn	Trp	Asp	Glu	Pro	Met	Asp	Tyr	Trp	Gly	Gln
			100					105					110		

Gly	Thr	Thr	Val	Thr	Val	Ser	Ser	Gly	Gly	Gly	Gly	Ser	Gly	Gly	Gly
		115					120					125			

Gly	Ser	Gly	Gly	Gly	Gly	Ser	Glu	Leu	Val	Met	Thr	Gln	Ser	Pro	Ser
	130					135					140				

Ser	Leu	Thr	Val	Thr	Ala	Gly	Glu	Lys	Val	Thr	Met	Ser	Cys	Lys	Ser
145					150					155					160

Ser Gln Ser Leu Leu₁₆₅ Asn Ser Gly Asn Gln₁₇₀ Lys Asn Tyr Leu Thr Trp
 Tyr Gln Gln Lys₁₈₀ Pro Gly Gln Pro Pro₁₈₅ Lys Leu Leu Ile Tyr Trp Ala
 Ser Thr Arg₁₉₅ Glu Ser Gly Val₂₀₀ Asp Arg Phe Thr Gly₂₀₅ Ser Gly Ser
 Gly Thr Asp Phe Thr Leu Thr₂₁₅ Ile Ser Ser Val₂₂₀ Gln Ala Glu Asp Leu
 Ala Val Tyr Tyr Cys Gln₂₃₀ Asn Asp Tyr Ser Tyr₂₃₅ Pro Leu Thr Phe Gly₂₄₀
 Ala Gly Thr Lys Leu₂₄₅ Glu Ile Lys Ser Gly₂₅₀ Gly Gly Gly Ser Asp Val
 Gln Leu Val Gln₂₆₀ Ser Gly Ala Glu Val₂₆₅ Lys Lys Pro Gly₂₇₀ Ala Ser Val
 Lys Val Ser₂₇₅ Cys Lys Ala Ser Gly₂₈₀ Tyr Thr Phe Thr Arg₂₈₅ Tyr Thr Met
 His Trp Val Arg Gln Ala Pro₂₉₅ Gly Gln Gly Leu Glu₃₀₀ Trp Ile Gly Tyr
 Ile Asn Pro Ser Arg Gly₃₁₀ Tyr Thr Asn Tyr Ala₃₁₅ Asp Ser Val Lys Gly₃₂₀
 Arg Phe Thr Ile Thr₃₂₅ Thr Asp Lys Ser Thr₃₃₀ Ser Thr Ala Tyr Met Glu₃₃₅
 Leu Ser Ser Leu₃₄₀ Arg Ser Glu Asp Thr₃₄₅ Ala Thr Tyr Tyr Cys₃₅₀ Ala Arg
 Tyr Tyr Asp₃₅₅ Asp His Tyr Cys Leu₃₆₀ Asp Tyr Trp Gly₃₆₅ Gln Gly Thr Thr
 Val Thr Val Ser Ser Gly Glu₃₇₅ Gly Thr Ser Thr Gly₃₈₀ Ser Gly Gly Ser
 Gly Gly Ser Gly Gly Ala₃₉₀ Asp Asp Ile Val Leu₃₉₅ Thr Gln Ser Pro Ala₄₀₀
 Thr Leu Ser Leu Ser₄₀₅ Pro Gly Glu Arg Ala₄₁₀ Thr Leu Thr Cys Arg Ala₄₁₅
 Ser Ser Ser Val₄₂₀ Ser Tyr Met Asn Trp₄₂₅ Tyr Gln Gln Lys Pro Gly Lys₄₃₀

Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser Gly Val
 435 440 445

Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr
 450 455 460

Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys Gln Gln
 465 470 475 480

Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile
 485 490 495

Lys

<210> 254

<211> 1488

<212> DNA

<213> artificial sequence

<220>

<223> 5-10VL3VH5 LHLH

<400> 254

gagctcgtga tgacacagtc tccatcctcc ctgactgtga cagcaggaga gaaggctcact	60
atgagctgca agtccagtca gagtctgtta aacagtggaa atcaaaagaa ctacttgacc	120
tggtaccagc agaaaccagg gcagcctcct aaactgttga tctactgggc atccactagg	180
gaatctgggg tccctgatcg cttcacaggc agtggatctg gaacagattt cactctcacc	240
atcagcagtg tgcaggctga agacctggca gtttattact gtcagaatga ttatagttat	300
ccgctcacgt tcggtgctgg gaccaagctt gagatcaaag gtggtggtgg ttctggcggc	360
ggcggctccg gtggtggtgg ttctgaggtg cagctgctcg agcagtctgg agctgagctg	420
gtaaggcctg ggacttcagt gaagatatcc tgcaaggctt ctggatacgc cttcactaac	480
tactggctag gttgggtaaa gcagaggcct ggacatggac ttgagtggat tggagatatt	540
ttccctggaa gtggtaatat ccactacaat gagaagttca agggcaaagc cacactgact	600
gcagacaaat cttcgagcac agcctatatg cagctcagta gcctgacatt tgaggactct	660
gctgtctatt tctgtgcaag actgaggaac tgggacgagc ctatggacta ctggggccaa	720
gggaccacgg tcaccgtctc ctccggaggt ggtggatccg acattgtact gaccagctct	780
ccagcaactc tgtctctgtc tccagggggag cgtgccaccc tgacctgcag agccagttca	840
agtgtaaagt acatgaactg gtaccagcag aagccgggca aggcacccaa aagatggatt	900
tatgacacat ccaaagtggc ttctggagtc cctgctcgct tcagtggcag tgggtctggg	960
accgactact ctctcacaat caacagcttg gaggctgaag atgctgccac ttattactgc	1020

caacagtgga gtagtaaccc gctcacgttc ggtggcggga ccaaggtgga gatcaaaggc 1080
 gaaggtacta gtactgggttc tgggtggaagt ggaggttcag gtggagcaga cgacgtccaa 1140
 ctggtgcagt caggggctga agtgaaaaaa cctggggcct cagtgaaggt gtcctgcaag 1200
 gcttctggct acacctttac taggtacacg atgcactggg taaggcaggc acctggacag 1260
 ggtctggaat ggattggata cattaatcct agccgtgggt atactaatta cgcagacagc 1320
 gtcaagggcc gcttcacaat cactacagac aaatccacca gcacagccta catggaactg 1380
 agcagcctgc gttctgagga cactgcaacc tattactgtg caagatatta tgatgatcat 1440
 tactgccttg actactgggg ccaaggcacc acggtcaccg tctcctca 1488

<210> 255

<211> 496

<212> PRT

<213> artificial sequence

<220>

<223> 5-10VL3VH5 LHLH

<400> 255

Glu Leu Val Met Thr Gln Ser Pro Ser Ser Leu Thr Val Thr Ala Gly
 1 5 10 15

Glu Lys Val Thr Met Ser Cys Lys Ser Ser Gln Ser Leu Leu Asn Ser
 20 25 30

Gly Asn Gln Lys Asn Tyr Leu Thr Trp Tyr Gln Gln Lys Pro Gly Gln
 35 40 45

Pro Pro Lys Leu Leu Ile Tyr Trp Ala Ser Thr Arg Glu Ser Gly Val
 50 55 60

Pro Asp Arg Phe Thr Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
 65 70 75 80

Ile Ser Ser Val Gln Ala Glu Asp Leu Ala Val Tyr Tyr Cys Gln Asn
 85 90 95

Asp Tyr Ser Tyr Pro Leu Thr Phe Gly Ala Gly Thr Lys Leu Glu Ile
 100 105 110

Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
 115 120 125

Glu Val Gln Leu Leu Glu Gln Ser Gly Ala Glu Leu Val Arg Pro Gly
 130 135 140

Thr Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Thr Asn
145 150 155 160

Tyr Trp Leu Gly Trp Val Lys Gln Arg Pro Gly His Gly Leu Glu Trp
165 170 175

Ile Gly Asp Ile Phe Pro Gly Ser Gly Asn Ile His Tyr Asn Glu Lys
180 185 190

Phe Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala
195 200 205

Tyr Met Gln Leu Ser Ser Leu Thr Phe Glu Asp Ser Ala Val Tyr Phe
210 215 220

Cys Ala Arg Leu Arg Asn Trp Asp Glu Pro Met Asp Tyr Trp Gly Gln
225 230 235 240

Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp Ile Val
245 250 255

Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala
260 265 270

Thr Leu Thr Cys Arg Ala Ser Ser Ser Val Ser Tyr Met Asn Trp Tyr
275 280 285

Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser
290 295 300

Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly
305 310 315 320

Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala
325 330 335

Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly
340 345 350

Gly Thr Lys Val Glu Ile Lys Gly Glu Gly Thr Ser Thr Gly Ser Gly
355 360 365

Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Val Gln Leu Val Gln Ser
370 375 380

Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys
385 390 395 400

Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp Val Arg Gln
405 410 415

Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn Pro Ser Arg
420 425 219 430

Gly Tyr Thr Asn Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Thr
435 440 445

Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg
450 455 460

Ser Glu Asp Thr Ala Thr Tyr Tyr Cys Ala Arg Tyr Tyr Asp Asp His
465 470 475 480

Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
485 490 495

<210> 256

<211> 1491

<212> DNA

<213> artificial sequence

<220>

<223> 5-10VL3VH5 HLLH

<400> 256

gaggtgcagc tgctcgagca gtctggagct gagctggtaa ggcctgggac ttcagtgaag	60
atatacctgca aggccttctgg atacgccttc actaactact ggctaggttg ggtaaagcag	120
aggcctggac atggacttga gtggattgga gatattttcc ctggaagtgg taatatccac	180
tacaatgaga agttcaaggg caaagccaca ctgactgcag acaaactctc gagcacagcc	240
tatatgcagc tcagtagcct gacatttgag gactctgctg tctattttctg tgcaagactg	300
aggaactggg acgagcctat ggactactgg ggccaagggg ccacgggtcac cgtctcctca	360
ggtaggtggtg gttctggcgg cggcggctcc ggtggtggtg gttctgagct cgtgatgaca	420
cagtctccat cctccctgac tgtgacagca ggagagaagg tcactatgag ctgcaagtcc	480
agtcagagtc tgtaaagcag tggaaatcaa aagaactact tgacctggtg ccagcagaaa	540
ccagggcagc ctctaaact gttgatctac tgggcatcca ctagggaatc tgggggtccct	600
gatcgcttca caggcagtgg atctggaaca gatttcactc tcaccatcag cagtgtgcag	660
gctgaagacc tggcagttta ttactgtcag aatgattata gttatccgct cacgttcggt	720
gctgggacca agcttgagat caaatccgga ggtggtggat ccgacattgt actgacctag	780
tctccagcaa ctctgtctct gtctccaggg gagcgtgcc ccctgacctg cagagccagt	840
tcaagtgtaa gttacatgaa ctggtaccag cagaagccgg gcaaggcacc caaaagatgg	900
atztatgaca catccaaagt ggcttctgga gtccctgctc gcttcagtgg cagtgggtct	960
gggaccgact actctctcac aatcaacagc ttggaggctg aagatgctgc cacttattac	1020

220

tgccaacagt ggagtagtaa cccgctcacg ttcggtggcg ggaccaaggt ggagatcaaa	1080
ggcgaaggta ctagtactgg ttctggtgga agtggagggt caggtggagc agacgacgtc	1140
caactggtgc agtcaggggc tgaagtgaaa aaacctgggg cctcagtgaa ggtgtcctgc	1200
aaggcttctg gctacacctt tactaggtac acgatgcact gggtaaggca ggcacctgga	1260
cagggtctgg aatggattgg atacattaat cctagccgtg gttatactaa ttacgcagac	1320
agcgtcaagg gccgcttcac aatcactaca gacaaatcca ccagcacagc ctacatggaa	1380
ctgagcagcc tgcgttctga ggacactgca acctattact gtgcaagata ttatgatgat	1440
cattactgcc ttgactactg gggccaaggc accacgggtca ccgtctcctc a	1491

<210> 257

<211> 497

<212> PRT

<213> artificial sequence

<220>

<223> 5-10VL3VH5 HLLH

<400> 257

Glu	Val	Gln	Leu	Leu	Glu	Gln	Ser	Gly	Ala	Glu	Leu	Val	Arg	Pro	Gly
1			5						10					15	

Thr	Ser	Val	Lys	Ile	Ser	Cys	Lys	Ala	Ser	Gly	Tyr	Ala	Phe	Thr	Asn
			20					25					30		

Tyr	Trp	Leu	Gly	Trp	Val	Lys	Gln	Arg	Pro	Gly	His	Gly	Leu	Glu	Trp
		35					40					45			

Ile	Gly	Asp	Ile	Phe	Pro	Gly	Ser	Gly	Asn	Ile	His	Tyr	Asn	Glu	Lys
	50					55					60				

Phe	Lys	Gly	Lys	Ala	Thr	Leu	Thr	Ala	Asp	Lys	Ser	Ser	Ser	Thr	Ala
65					70					75					80

Tyr	Met	Gln	Leu	Ser	Ser	Leu	Thr	Phe	Glu	Asp	Ser	Ala	Val	Tyr	Phe
			85						90					95	

Cys	Ala	Arg	Leu	Arg	Asn	Trp	Asp	Glu	Pro	Met	Asp	Tyr	Trp	Gly	Gln
			100					105					110		

Gly	Thr	Thr	Val	Thr	Val	Ser	Ser	Gly	Gly	Gly	Gly	Ser	Gly	Gly	Gly
		115					120					125			

Gly	Ser	Gly	Gly	Gly	Gly	Ser	Glu	Leu	Val	Met	Thr	Gln	Ser	Pro	Ser
	130					135					140				

Ser₁₄₅ Leu Thr Val Thr Ala₁₅₀ Gly Glu Lys Val²²¹ Thr₁₅₅ Met Ser Cys Lys Ser₁₆₀
 Ser Gln Ser Leu Leu₁₆₅ Asn Ser Gly Asn Gln₁₇₀ Lys Asn Tyr Leu Thr₁₇₅ Trp
 Tyr Gln Gln Lys₁₈₀ Pro Gly Gln Pro Pro₁₈₅ Lys Leu Leu Ile Tyr Trp Ala₁₉₀
 Ser Thr Arg₁₉₅ Glu Ser Gly Val₂₀₀ Asp Arg Phe Thr Gly₂₀₅ Ser Gly Ser
 Gly Thr₂₁₀ Asp Phe Thr Leu Thr₂₁₅ Ile Ser Ser Val Gln₂₂₀ Ala Glu Asp Leu
 Ala Val Tyr Tyr Cys Gln₂₃₀ Asn Asp Tyr Ser Tyr₂₃₅ Pro Leu Thr Phe Gly₂₄₀
 Ala Gly Thr Lys Leu₂₄₅ Glu Ile Lys Ser Gly₂₅₀ Gly Gly Gly Ser Asp₂₅₅ Ile
 Val Leu Thr Gln₂₆₀ Ser Pro Ala Thr Leu₂₆₅ Ser Leu Ser Pro Gly₂₇₀ Glu Arg
 Ala Thr Leu₂₇₅ Thr Cys Arg Ala Ser₂₈₀ Ser Ser Val Ser Tyr₂₈₅ Met Asn Trp
 Tyr Gln₂₉₀ Gln Lys Pro Gly Lys₂₉₅ Ala Pro Lys Arg Trp₃₀₀ Ile Tyr Asp Thr
 Ser₃₀₅ Lys Val Ala Ser Gly₃₁₀ Val Pro Ala Arg Phe₃₁₅ Ser Gly Ser Gly Ser₃₂₀
 Gly Thr Asp Tyr Ser₃₂₅ Leu Thr Ile Asn Ser₃₃₀ Leu Glu Ala Glu Asp₃₃₅ Ala
 Ala Thr Tyr Tyr₃₄₀ Cys Gln Gln Trp Ser₃₄₅ Ser Asn Pro Leu Thr Phe Gly
 Gly Gly Thr₃₅₅ Lys Val Glu Ile Lys₃₆₀ Gly Glu Gly Thr Ser₃₆₅ Thr Gly Ser
 Gly Gly Ser Gly Gly Ser Gly₃₇₅ Gly Ala Asp Asp Val₃₈₀ Gln Leu Val Gln
 Ser₃₈₅ Gly Ala Glu Val Lys₃₉₀ Lys Pro Gly Ala Ser₃₉₅ Val Lys Val Ser Cys₄₀₀
 Lys Ala Ser Gly Tyr₄₀₅ Thr Phe Thr Arg Tyr₄₁₀ Thr Met His Trp Val Arg₄₁₅
 Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn Pro Ser

420 222 430
 Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile
 435 440 445
 Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser Ser Leu
 450 455 460
 Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys Ala Arg Tyr Tyr Asp Asp
 465 470 475 480
 His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser
 485 490 495

Ser

<210> 258
 <211> 1488
 <212> DNA
 <213> artificial sequence

<220>

<223> 5-10VH7VL1 LHHL

<400> 258
 gagctcgtga tgacacagtc tccatcctcc ctgactgtga cagcaggaga gaaggctcact 60
 atgagctgca agtccagtc gagtctgtta aacagtggaa atcaaaagaa ctacttgacc 120
 tgggtaccagc agaaaccagg gcagcctcct aaactgttga tctactgggc atccactagg 180
 gaatctgggg tccctgatcg cttcacaggc agtggatctg gaacagattt cactctcacc 240
 atcagcagtg tgcaggctga agacctggca gtttattact gtcagaatga ttatagttat 300
 ccgctcacgt tcggtgctgg gaccaagctt gagatcaaag gtggtggtgg ttctggcggc 360
 ggcggctccg gtggtggtgg ttctgaggtg cagctgctcg agcagtctgg agctgagctg 420
 gtaaggcctg ggacttcagt gaagatatcc tgcaaggctt ctggatacgc cttcactaac 480
 tactggctag gttgggtaaa gcagaggcct ggacatggac ttgagtggat tggagatatt 540
 ttccctggaa gtggtaatat ccactacaat gagaagttca agggcaaagc cacactgact 600
 gcagacaaat cttcgagcac agcctatatg cagctcagta gcctgacatt tgaggactct 660
 gctgtctatt tctgtgcaag actgaggaac tgggacgagc ctatggacta ctggggccaa 720
 gggaccacgg tcaccgtctc ctccggaggt ggtggatccg acgtccaact ggtgcagtca 780
 ggggctgaag tgaaaaaacc tggggcctca gtgaagggtgt cctgcaaggc ttctggctac 840
 acctttacta ggtacacgat gcactgggta aggcaggcac ctggacaggg tctggaatgg 900
 attggataca ttaatcctag ccgtgggttat actaattaca atcagaagtt caaggaccgc 960

gtcacaatca ctacagacaa atccaccagc acagcctaca tggaactgag cagcctgcgt 1020
 tctgaggaca ctgcagtcta ttactgtgca agatattatg atgatcatta ctgccttgac 1080
 tactggggcc aaggcaccac ggtcaccgtc tcctcaggcg aaggtactag tactgggttct 1140
 ggtggaagtg gaggttcagg tggagcagac gacattcaga tgaccagtc tccatctagc 1200
 ctgtctgcat ctgtcgggga ccgtgtcacc atcacctgca gagccagtca aagtgttaagt 1260
 tacatgaact ggtaccagca gaagccgggc aaggcaccca aaagatggat ttatgacaca 1320
 tccaaagtgg cttctggagt ccctgctcgc ttcagtggca gtgggtctgg gaccgactac 1380
 tctctcacia tcaacagctt ggaggctgaa gatgctgcca cttattactg ccaacagtgg 1440
 agtagtaacc cgctcacgtt cggtggcggg accaaggtgg agatcaaa 1488

<210> 259

<211> 496

<212> PRT

<213> artificial sequence

<220>

<223> 5-10VH7VL1 LHHL

<400> 259

Glu Leu Val Met Thr Gln Ser Pro Ser Ser Leu Thr Val Thr Ala Gly
 1 5 10 15

Glu Lys Val Thr Met Ser Cys Lys Ser Ser Gln Ser Leu Leu Asn Ser
 20 25 30

Gly Asn Gln Lys Asn Tyr Leu Thr Trp Tyr Gln Gln Lys Pro Gly Gln
 35 40 45

Pro Pro Lys Leu Leu Ile Tyr Trp Ala Ser Thr Arg Glu Ser Gly Val
 50 55 60

Pro Asp Arg Phe Thr Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
 65 70 75 80

Ile Ser Ser Val Gln Ala Glu Asp Leu Ala Val Tyr Tyr Cys Gln Asn
 85 90 95

Asp Tyr Ser Tyr Pro Leu Thr Phe Gly Ala Gly Thr Lys Leu Glu Ile
 100 105 110

Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
 115 120 125

Glu Val Gln Leu Leu Glu Gln Ser Gly Ala Glu Leu Val Arg Pro Gly

130 135 224 140
 Thr Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Thr Asn
 145 150 155 160
 Tyr Trp Leu Gly Trp Val Lys Gln Arg Pro Gly His Gly Leu Glu Trp
 165 170 175
 Ile Gly Asp Ile Phe Pro Gly Ser Gly Asn Ile His Tyr Asn Glu Lys
 180 185 190
 Phe Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala
 195 200 205
 Tyr Met Gln Leu Ser Ser Leu Thr Phe Glu Asp Ser Ala Val Tyr Phe
 210 215 220
 Cys Ala Arg Leu Arg Asn Trp Asp Glu Pro Met Asp Tyr Trp Gly Gln
 225 230 235 240
 Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp Val Gln
 245 250 255
 Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys
 260 265 270
 Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His
 275 280 285
 Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile
 290 295 300
 Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe Lys Asp Arg
 305 310 315 320
 Val Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu
 325 330 335
 Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Tyr
 340 345 350
 Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val
 355 360 365
 Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly Gly Ser Gly
 370 375 380
 Gly Ser Gly Gly Ala Asp Asp Ile Gln Met Thr Gln Ser Pro Ser Ser
 385 390 395 400
 Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser
 405 410 415

Gln Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala
 420 425 430

Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser Gly Val Pro
 435 440 445

Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile
 450 455 460

Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp
 465 470 475 480

Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
 485 490 495

<210> 260

<211> 1491

<212> DNA

<213> artificial sequence

<220>

<223> 5-10VH7VL1 HLHL

<400> 260

gagggtgcagc tgctcgagca gtctggagct gagctggtaa ggcctgggac ttcagtgaag	60
atatacctgca aggcttctgg atacgccttc actaactact ggctagggttg ggtaaagcag	120
aggcctggac atggacttga gtggattgga gatattttcc ctggaagtgg taatatccac	180
tacaatgaga agttcaaggg caaagccaca ctgactgcag acaaatcttc gagcacagcc	240
tatatgcagc tcagtagcct gacatttgag gactctgctg tctattttctg tgcaagactg	300
aggaactggg acgagcctat ggactactgg ggccaagggg ccacgggtcac cgtctcctca	360
ggtggtggtg gttctggcgg cggcggtcc ggtggtggtg gttctgagct cgtgatgaca	420
cagtctccat cctccctgac tgtgacagca ggagagaagg tcactatgag ctgcaagtcc	480
agtcagagtc tgtaaacag tggaaatcaa aagaactact tgacctggta ccagcagaaa	540
ccagggcagc ctctaaact gttgatctac tgggcatcca ctagggaatc tggggtcct	600
gatcgcttca caggcagtgg atctggaaca gatttcactc tcaccatcag cagtgtgcag	660
gctgaagacc tggcagttta ttactgtcag aatgattata gttatccgct cacgttcggt	720
gctgggacca agcttgagat caaatccgga ggtggtggat ccgacgtcca actggtgcag	780
tcaggggctg aagtgaaaaa acctggggcc tcagtgaagg tgtcctgcaa ggcttctggc	840
tacaccttta ctaggtacac gatgcactgg gtaaggcagg cacctggaca gggctctggaa	900
tggattggat acattaatcc tagccgtggt tataactaatt acaatcagaa gttcaaggac	960

226

cgcgtcacaa tcactacaga caaatccacc agcacagcct acatggaact gagcagcctg	1020
cgttctgagg aactgcagt ctattactgt gcaagatatt atgatgatca ttactgcctt	1080
gactactggg gccaaaggcac cacggtcacc gtctcctcag gcgaagggtac tagtactggt	1140
tctgggtggaa gtggagggttc aggtggagca gacgacattc agatgaccca gtctccatct	1200
agcctgtctg catctgtcgg ggaccgtgtc accatcacct gcagagccag tcaaagtgta	1260
agttacatga actggtacca gcagaagccg ggcaaggcac caaaagatg gatttatgac	1320
acatccaaag tggcttctgg agtccctgct cgcttcagtgc gcagtgggtc tgggaccgac	1380
tactctctca caatcaacag cttggaggct gaagatgctg ccacttatta ctgccaacag	1440
tggagtagta acccgctcac gttcggtggc gggaccaagg tggagatcaa a	1491

<210> 261

<211> 497

<212> PRT

<213> artificial sequence

<220>

<223> 5-10VH7VL1 HLHL

<400> 261

Glu	Val	Gln	Leu	Leu	Glu	Gln	Ser	Gly	Ala	Glu	Leu	Val	Arg	Pro	Gly
1			5						10					15	

Thr	Ser	Val	Lys	Ile	Ser	Cys	Lys	Ala	Ser	Gly	Tyr	Ala	Phe	Thr	Asn
			20					25					30		

Tyr	Trp	Leu	Gly	Trp	Val	Lys	Gln	Arg	Pro	Gly	His	Gly	Leu	Glu	Trp
		35					40					45			

Ile	Gly	Asp	Ile	Phe	Pro	Gly	Ser	Gly	Asn	Ile	His	Tyr	Asn	Glu	Lys
	50					55					60				

Phe	Lys	Gly	Lys	Ala	Thr	Leu	Thr	Ala	Asp	Lys	Ser	Ser	Ser	Thr	Ala
65					70					75					80

Tyr	Met	Gln	Leu	Ser	Ser	Leu	Thr	Phe	Glu	Asp	Ser	Ala	Val	Tyr	Phe
				85					90					95	

Cys	Ala	Arg	Leu	Arg	Asn	Trp	Asp	Glu	Pro	Met	Asp	Tyr	Trp	Gly	Gln
			100					105					110		

Gly	Thr	Thr	Val	Thr	Val	Ser	Ser	Gly	Gly	Gly	Gly	Ser	Gly	Gly	Gly
		115					120					125			

Gly	Ser	Gly	Gly	Gly	Gly	Ser	Glu	Leu	Val	Met	Thr	Gln	Ser	Pro	Ser
	130					135					140				

Ser Leu Thr Val Thr Ala Gly Glu Lys Val Thr Met Ser Cys Lys Ser
145 150 155 160

Ser Gln Ser Leu Leu Asn Ser Gly Asn Gln Lys Asn Tyr Leu Thr Trp
165 170 175

Tyr Gln Gln Lys Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr Trp Ala
180 185 190

Ser Thr Arg Glu Ser Gly Val Pro Asp Arg Phe Thr Gly Ser Gly Ser
195 200 205

Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Val Gln Ala Glu Asp Leu
210 215 220

Ala Val Tyr Tyr Cys Gln Asn Asp Tyr Ser Tyr Pro Leu Thr Phe Gly
225 230 235 240

Ala Gly Thr Lys Leu Glu Ile Lys Ser Gly Gly Gly Gly Ser Asp Val
245 250 255

Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val
260 265 270

Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met
275 280 285

His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr
290 295 300

Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe Lys Asp
305 310 315 320

Arg Val Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu
325 330 335

Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg
340 345 350

Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr
355 360 365

Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly Gly Ser
370 375 380

Gly Gly Ser Gly Gly Ala Asp Asp Ile Gln Met Thr Gln Ser Pro Ser
385 390 395 400

Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala
405 410 415

Ser Gln Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro Gly Lys
 420 425 430

Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser Gly Val
 435 440 445

Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr
 450 455 460

Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys Gln Gln
 465 470 475 480

Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile
 485 490 495

Lys

<210> 262

<211> 1488

<212> DNA

<213> artificial sequence

<220>

<223> 5-10VL1VH7 LHLH

<400> 262

gagctcgtga tgacacagtc tccatcctcc ctgactgtga cagcaggaga gaaggtcact	60
atgagctgca agtccagtca gagtctgtta aacagtggaa atcaaaagaa ctacttgacc	120
tggtaccagc agaaaccagg gcagcctcct aaactgttga tctactgggc atccactagg	180
gaatctgggg tccctgatcg cttcacaggc agtggatctg gaacagattt cactctcacc	240
atcagcagtg tgcaggctga agacctggca gtttattact gtcagaatga ttatagttat	300
ccgctcacgt tcggtgctgg gaccaagctt gagatcaaag gtggtggtgg ttctggcggc	360
ggcggctccg gtggtggtgg ttctgaggtg cagctgctcg agcagtctgg agctgagctg	420
gtaaggcctg ggacttcagt gaagatatcc tgcaaggctt ctggatacgc cttcactaac	480
tactggctag gttgggtaaa gcagaggcct ggacatggac ttgagtggat tggagatatt	540
ttccctggaa gtggtaatat ccactacaat gagaagttca agggcaaagc cacactgact	600
gcagacaaat cttcgagcac agcctatatg cagctcagta gcctgacatt tgaggactct	660
gctgtctatt tctgtgcaag actgaggaac tgggacgagc ctatggacta ctggggccaa	720
gggaccacgg tcaccgtctc ctccggaggt ggtggatccg acattcagat gaccagctct	780
ccatctagcc tgtctgcatc tgtcggggac cgtgtcacca tcacctgcag agccagtcaa	840
agtgtaagtt acatgaactg gtaccagcag aagccgggca aggcacccaa aagatggatt	900

tatgacacat ccaaagtggc ttctggagtc cctgctcgct tcagtggcag tgggtctggg 960
 accgactact ctctcacaat caacagcttg gaggtgaag atgctgccac ttattactgc 1020
 caacagtgga gtagtaaccc gctcacgttc ggtggcgga ccaaggtgga gatcaaaggc 1080
 gaaggtacta gtactgggtc tgggtggaagt ggaggttcag gtggagcaga cgacgtccaa 1140
 ctggtgcagt caggggctga agtgaaaaaa cctggggcct cagtgaaggt gtcctgcaag 1200
 gcttctggct acacctttac taggtacacg atgcactggg taaggcaggc acctggacag 1260
 ggtctggaat ggattggata cattaatcct agccgtgggt atactaatta caatcagaag 1320
 ttcaaggacc gcgtcacaat cactacagac aaatccacca gcacagccta catggaactg 1380
 agcagcctgc gttctgagga cactgcagtc tattactgtg caagatatta tgatgatcat 1440
 tactgccttg actactgggg ccaaggcacc acggtcaccg tctcctca 1488

<210> 263

<211> 496

<212> PRT

<213> artificial sequence

<220>

<223> 5-10VL1VH7 LHLH

<400> 263

Glu Leu Val Met Thr Gln Ser Pro Ser Ser Leu Thr Val Thr Ala Gly
 1 5 10 15

Glu Lys Val Thr Met Ser Cys Lys Ser Ser Gln Ser Leu Leu Asn Ser
 20 25 30

Gly Asn Gln Lys Asn Tyr Leu Thr Trp Tyr Gln Gln Lys Pro Gly Gln
 35 40 45

Pro Pro Lys Leu Leu Ile Tyr Trp Ala Ser Thr Arg Glu Ser Gly Val
 50 55 60

Pro Asp Arg Phe Thr Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
 65 70 75 80

Ile Ser Ser Val Gln Ala Glu Asp Leu Ala Val Tyr Tyr Cys Gln Asn
 85 90 95

Asp Tyr Ser Tyr Pro Leu Thr Phe Gly Ala Gly Thr Lys Leu Glu Ile
 100 105 110

Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
 115 120 125

230

Glu Val Gln Leu Leu Glu Gln Ser Gly Ala Glu Leu Val Arg Pro Gly
130 135 140

Thr Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Thr Asn
145 150 155 160

Tyr Trp Leu Gly Trp Val Lys Gln Arg Pro Gly His Gly Leu Glu Trp
165 170 175

Ile Gly Asp Ile Phe Pro Gly Ser Gly Asn Ile His Tyr Asn Glu Lys
180 185 190

Phe Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala
195 200 205

Tyr Met Gln Leu Ser Ser Leu Thr Phe Glu Asp Ser Ala Val Tyr Phe
210 215 220

Cys Ala Arg Leu Arg Asn Trp Asp Glu Pro Met Asp Tyr Trp Gly Gln
225 230 235 240

Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp Ile Gln
245 250 255

Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val
260 265 270

Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Ser Tyr Met Asn Trp Tyr
275 280 285

Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser
290 295 300

Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly
305 310 315 320

Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala
325 330 335

Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly
340 345 350

Gly Thr Lys Val Glu Ile Lys Gly Glu Gly Thr Ser Thr Gly Ser Gly
355 360 365

Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Val Gln Leu Val Gln Ser
370 375 380

Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys
385 390 395 400

Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp val Arg Gln
405 410 415

Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn Pro Ser Arg
420 425 430

Gly Tyr Thr Asn Tyr Asn Gln Lys Phe Lys Asp Arg Val Thr Ile Thr
435 .440 445

Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg
450 455 460

Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Tyr Tyr Asp Asp His
465 470 475 480

Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
485 490 495

<210> 264

<211> 1491

<212> DNA

<213> artificial sequence

<220>

<223> 5-10VL1VH7 HLLH

<400> 264

gaggtgcagc	tgctcgagca	gtctggagct	gagctggtaa	ggcctgggac	ttcagtgaag	60
atatcctgca	aggcttctgg	atacgccctt	actaactact	ggctaggttg	ggtaaagcag	120
aggcctggac	atggacttga	gtggattgga	gatattttcc	ctggaagtgg	taatatccac	180
tacaatgaga	agttcaaggg	caaagccaca	ctgactgcag	acaaatcttc	gagcacagcc	240
tatatgcagc	tcagtagcct	gacatttgag	gactctgctg	tctattttctg	tgcaagactg	300
aggaactggg	acgagcctat	ggactactgg	ggccaagggg	ccacggtcac	cgtctcctca	360
ggtggtggtg	gttctggcgg	cggcggctcc	ggtggtggtg	gttctgagct	cgtgatgaca	420
cagtctccat	cctccctgac	tgtgacagca	ggagagaagg	tcactatgag	ctgcaagtcc	480
agtcagagtc	tgttaaacag	tggaaatcaa	aagaactact	tgacctggta	ccagcagaaa	540
ccagggcagc	ctcctaaact	gttgatctac	tgggcatcca	ctaggggaatc	tgggggtccct	600
gatcgcttca	caggcagtgg	atctggaaca	gattttcactc	tcaccatcag	cagtgtgcag	660
gctgaagacc	tggcagttta	ttactgtcag	aatgattata	gttatccgct	cacgttcggt	720
gctgggacca	agcttgagat	caaatccgga	ggtggtggat	ccgacattca	gatgaccag	780
tctccatcta	gcctgtctgc	atctgtcggg	gaccgtgtca	ccatcacctg	cagagccagt	840
caaagtgtaa	gttacatgaa	ctggtaccag	cagaagccgg	gcaaggcacc	caaaagatgg	900

232

atttatgaca catccaaagt ggcttctgga gtccctgctc gcttcagtgg cagtgggtct	960
gggaccgact actctctcac aatcaacagc ttggaggctg aagatgctgc cacttattac	1020
tgccaacagt ggagtagtaa cccgctcacg ttcggtggcg ggaccaaggt ggagatcaaa	1080
ggcgaaggta ctagtactgg ttctggtgga agtggagggt cagggtggagc agacgacgtc	1140
caactggtgc agtcaggggc tgaagtgaaa aaacctgggg cctcagtga ggtgtcctgc	1200
aaggcttctg gctacacctt tactaggtac acgatgcact gggtaaggca ggcacctgga	1260
cagggtctgg aatggattgg atacattaat cctagccgtg gttataactaa ttacaatcag	1320
aagttcaagg accgcgtcac aatcactaca gacaaatcca ccagcacagc ctacatggaa	1380
ctgagcagcc tgcgttctga ggacactgca gtctattact gtgcaagata ttatgatgat	1440
cattactgcc ttgactactg gggccaaggc accacgggtca ccgtctcctc a	1491

<210> 265

<211> 497

<212> PRT

<213> artificial sequence

<220>

<223> 5-10VL1VH7 HLLH

<400> 265

Glu	Val	Gln	Leu	Leu	Glu	Gln	Ser	Gly	Ala	Glu	Leu	Val	Arg	Pro	Gly
1				5					10					15	

Thr	Ser	Val	Lys	Ile	Ser	Cys	Lys	Ala	Ser	Gly	Tyr	Ala	Phe	Thr	Asn
			20					25					30		

Tyr	Trp	Leu	Gly	Trp	Val	Lys	Gln	Arg	Pro	Gly	His	Gly	Leu	Glu	Trp
		35					40					45			

Ile	Gly	Asp	Ile	Phe	Pro	Gly	Ser	Gly	Asn	Ile	His	Tyr	Asn	Glu	Lys
	50					55					60				

Phe	Lys	Gly	Lys	Ala	Thr	Leu	Thr	Ala	Asp	Lys	Ser	Ser	Ser	Thr	Ala
65					70					75					80

Tyr	Met	Gln	Leu	Ser	Ser	Leu	Thr	Phe	Glu	Asp	Ser	Ala	Val	Tyr	Phe
				85					90					95	

Cys	Ala	Arg	Leu	Arg	Asn	Trp	Asp	Glu	Pro	Met	Asp	Tyr	Trp	Gly	Gln
			100					105					110		

Gly	Thr	Thr	Val	Thr	Val	Ser	Ser	Gly	Gly	Gly	Gly	Ser	Gly	Gly	Gly
			115				120					125			

Gly Ser Gly Gly Gly Gly Ser Glu Leu Val²³³ Met Thr Gln Ser Pro Ser
 130 135 140
 Ser Leu Thr Val Thr Ala Gly Glu Lys Val Thr Met Ser Cys Lys Ser
 145 150 155 160
 Ser Gln Ser Leu Leu Asn Ser Gly Asn Gln Lys Asn Tyr Leu Thr Trp
 165 170 175
 Tyr Gln Gln Lys Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr Trp Ala
 180 185 190
 Ser Thr Arg Glu Ser Gly Val Pro Asp Arg Phe Thr Gly Ser Gly Ser
 195 200 205
 Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Val Gln Ala Glu Asp Leu
 210 215 220
 Ala Val Tyr Tyr Cys Gln Asn Asp Tyr Ser Tyr Pro Leu Thr Phe Gly
 225 230 235 240
 Ala Gly Thr Lys Leu Glu Ile Lys Ser Gly Gly Gly Gly Ser Asp Ile
 245 250 255
 Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg
 260 265 270
 Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Ser Tyr Met Asn Trp
 275 280 285
 Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr
 290 295 300
 Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser
 305 310 315 320
 Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala
 325 330 335
 Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly
 340 345 350
 Gly Gly Thr Lys Val Glu Ile Lys Gly Glu Gly Thr Ser Thr Gly Ser
 355 360 365
 Gly Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Val Gln Leu Val Gln
 370 375 380
 Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys
 385 390 395 400
 Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp Val Arg

				405						234							415
Gln	Ala	Pro	Gly 420	Gln	Gly	Leu	Glu	Trp 425	Ile	Gly	Tyr	Ile	Asn 430	Pro	Ser		
Arg	Gly	Tyr 435	Thr	Asn	Tyr	Asn	Gln 440	Lys	Phe	Lys	Asp	Arg 445	Val	Thr	Ile		
Thr	Thr 450	Asp	Lys	Ser	Thr	Ser 455	Thr	Ala	Tyr	Met	Glu 460	Leu	Ser	Ser	Leu		
Arg 465	Ser	Glu	Asp	Thr	Ala 470	Val	Tyr	Tyr	Cys	Ala 475	Arg	Tyr	Tyr	Asp	Asp 480		
His	Tyr	Cys	Leu	Asp 485	Tyr	Trp	Gly	Gln	Gly 490	Thr	Thr	Val	Thr	Val 495	Ser		

Ser

<210> 266

<211> 1488

<212> DNA

<213> artificial sequence

<220>

<223> 5-10/VH7VL2 LHHL

<400>	266						
gagctcgtga	tgacacagtc	tccatcctcc	ctgactgtga	cagcaggaga	gaagggtcact		60
atgagctgca	agtccagtc	gagtctgtta	aacagtggaa	atcaaaagaa	ctacttgacc		120
tggtaccagc	agaaaccagg	gcagcctcct	aaactgttga	tctactgggc	atccactagg		180
gaatctgggg	tccctgatcg	cttcacaggc	agtggatctg	gaacagattt	cactctcacc		240
atcagcagtg	tgcaggctga	agacctggca	gtttattact	gtcagaatga	ttatagttat		300
ccgctcacgt	tcggtgctgg	gaccaagctt	gagatcaaag	gtggtggtgg	ttctggcggc		360
ggcggctccg	gtggtggtgg	ttctgaggtg	cagctgctcg	agcagtctgg	agctgagctg	--	420
gtaaggcctg	ggacttcagt	gaagatatcc	tgcaaggctt	ctggatacgc	cttcactaac		480
tactggctag	gttgggtaaa	gcagaggcct	ggacatggac	ttgagtggat	tggagatatt		540
ttccctggaa	gtggtaatat	ccactacaat	gagaagttca	agggcaaagc	cacactgact		600
gcagacaaat	cttcgagcac	agcctatatg	cagctcagta	gcctgacatt	tgaggactct		660
gctgtctatt	tctgtgcaag	actgaggaac	tgggacgagc	ctatggacta	ctggggccaa		720
gggaccacgg	tcaccgtctc	ctccggaggt	ggtggatccg	acgtccaact	ggtgcagtca		780
ggggctgaag	tgaaaaaacc	tggggcctca	gtgaagggtgt	cctgcaaggc	ttctggctac		840

acctttacta ggtacacgat gcactgggta aggcaggcac ctggacaggg tctggaatgg 900
 attggataca ttaatcctag ccgtgggttat actaattaca atcagaagtt caaggaccgc 960
 gtcacaatca ctacagacaa atccaccagc acagcctaca tggaactgag cagcctgcgt 1020
 tctgaggaca ctgcagtcta ttactgtgca agatattatg atgatcatta ctgccttgac 1080
 tactggggcc aaggcaccac ggtcaccgtc tcctcaggcg aaggtactag tactgggttct 1140
 ggtggaagtg gaggttcagg tggagcagac gacattgtac tgaccagtc tccagcaact 1200
 ctgtctctgt ctccagggga gcgtgccacc ctgagctgca gagccagtca aagtgttaagt 1260
 tacatgaact ggtaccagca gaagccgggc aaggcaccca aaagatggat ttatgacaca 1320
 tccaaagtgg cttctggagt ccctgctcgc ttcagtggca gtgggtctgg gaccgactac 1380
 tctctcacia tcaacagctt ggaggctgaa gatgctgcca cttattactg ccaacagtgg 1440
 agtagtaacc cgctcacgtt cgggtggcggg accaaggtgg agatcaaa 1488

<210> 267

<211> 496

<212> PRT

<213> artificial sequence

<220>

<223> 5-10/VH7VL2 LHHL

<400> 267

Glu Leu Val Met Thr Gln Ser Pro Ser Ser Leu Thr Val Thr Ala Gly
 1 5 10 15

Glu Lys Val Thr Met Ser Cys Lys Ser Ser Gln Ser Leu Leu Asn Ser
 20 25 30

Gly Asn Gln Lys Asn Tyr Leu Thr Trp Tyr Gln Gln Lys Pro Gly Gln
 35 40 45

Pro Pro Lys Leu Leu Ile Tyr Trp Ala Ser Thr Arg Glu Ser Gly Val
 50 55 60

Pro Asp Arg Phe Thr Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
 65 70 75 80

Ile Ser Ser Val Gln Ala Glu Asp Leu Ala Val Tyr Tyr Cys Gln Asn
 85 90 95

Asp Tyr Ser Tyr Pro Leu Thr Phe Gly Ala Gly Thr Lys Leu Glu Ile
 100 105 110

Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Ser

115					120					236					125				
Glu	Val	Gln	Leu	Leu	Glu	Gln	Ser	Gly	Ala	Glu	Leu	Val	Arg	Pro	Gly				
	130					135					140								
Thr	Ser	Val	Lys	Ile	Ser	Cys	Lys	Ala	Ser	Gly	Tyr	Ala	Phe	Thr	Asn				
145					150					155					160				
Tyr	Trp	Leu	Gly	Trp	Val	Lys	Gln	Arg	Pro	Gly	His	Gly	Leu	Glu	Trp				
				165					170					175					
Ile	Gly	Asp	Ile	Phe	Pro	Gly	Ser	Gly	Asn	Ile	His	Tyr	Asn	Glu	Lys				
			180					185					190						
Phe	Lys	Gly	Lys	Ala	Thr	Leu	Thr	Ala	Asp	Lys	Ser	Ser	Ser	Thr	Ala				
		195					200					205							
Tyr	Met	Gln	Leu	Ser	Ser	Leu	Thr	Phe	Glu	Asp	Ser	Ala	Val	Tyr	Phe				
	210					215					220								
Cys	Ala	Arg	Leu	Arg	Asn	Trp	Asp	Glu	Pro	Met	Asp	Tyr	Trp	Gly	Gln				
225					230					235					240				
Gly	Thr	Thr	Val	Thr	Val	Ser	Ser	Gly	Gly	Gly	Gly	Ser	Asp	Val	Gln				
				245					250					255					
Leu	Val	Gln	Ser	Gly	Ala	Glu	Val	Lys	Lys	Pro	Gly	Ala	Ser	Val	Lys				
			260					265					270						
Val	Ser	Cys	Lys	Ala	Ser	Gly	Tyr	Thr	Phe	Thr	Arg	Tyr	Thr	Met	His				
		275					280					285							
Trp	Val	Arg	Gln	Ala	Pro	Gly	Gln	Gly	Leu	Glu	Trp	Ile	Gly	Tyr	Ile				
	290					295					300								
Asn	Pro	Ser	Arg	Gly	Tyr	Thr	Asn	Tyr	Asn	Gln	Lys	Phe	Lys	Asp	Arg				
305					310					315					320				
Val	Thr	Ile	Thr	Thr	Asp	Lys	Ser	Thr	Ser	Thr	Ala	Tyr	Met	Glu	Leu				
				325					330					335					
Ser	Ser	Leu	Arg	Ser	Glu	Asp	Thr	Ala	Val	Tyr	Tyr	Cys	Ala	Arg	Tyr				
			340					345					350						
Tyr	Asp	Asp	His	Tyr	Cys	Leu	Asp	Tyr	Trp	Gly	Gln	Gly	Thr	Thr	Val				
		355					360					365							
Thr	Val	Ser	Ser	Gly	Glu	Gly	Thr	Ser	Thr	Gly	Ser	Gly	Gly	Ser	Gly				
	370					375					380								
Gly	Ser	Gly	Gly	Ala	Asp	Asp	Ile	Val	Leu	Thr	Gln	Ser	Pro	Ala	Thr				
385					390					395					400				

Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser
405 410 415

Gln Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala
420 425 430

Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser Gly Val Pro
435 440 445

Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile
450 455 460

Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp
465 470 475 480

Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
485 490 495

<210> 268

<211> 1491

<212> DNA

<213> artificial sequence

<220>

<223> 5-10/VH7VL2 HLHL

<400> 268

gaggtgcagc tgctcgagca gtctggagct gagctggtaa ggcctgggac ttcagtgaag	60
atatcctgca aggcttctgg atacgccttc actaactact ggctagggtg ggtaaagcag	120
aggcctggac atggacttga gtggattgga gatattttcc ctggaagtgg taatatccac	180
tacaatgaga agttcaaggg caaagccaca ctgactgcag acaaatcttc gagcacagcc	240
tatatgcagc tcagtagcct gacatttgag gactctgctg tctatttctg tgcaagactg	300
aggaactggg acgagcctat ggactactgg ggccaaggga ccacggtcac cgtctcctca	360
ggtgggtggg gttctggcgg cggcggctcc ggtgggtggg gttctgagct cgtgatgaca	420
cagtctccat cctccctgac tgtgacagca ggagagaagg tcactatgag ctgcaagtcc	480
agtcagagtc tgtaaacag tggaaatcaa aagaactact tgacctggta ccagcagaaa	540
ccagggcagc ctctaaact gttgatctac tgggcatcca ctagggaatc tggggtcct	600
gatcgcttca caggcagtgg atctggaaca gatttcactc tcaccatcag cagtgtgcag	660
gctgaagacc tggcagttta ttactgtcag aatgattata gttatccgct cacgttcggt	720
gctgggacca agcttgagat caaatccgga ggtgggtggat ccgacgtcca actggtgcag	780
tcaggggctg aagtgaaaaa acctggggcc tcagtgaagg tgcctgcaa ggcttctggc	840

238

tacaccttta ctaggtacac gatgcactgg gtaaggcagg cacctggaca gggctctggaa	900
tggattggat acattaatcc tagccgtgggt tataactaatt acaatcagaa gttcaaggac	960
cgcgtcacaa tcactacaga caaatccacc agcacagcct acatggaact gagcagcctg	1020
cgttctgagg aactgcagt ctattactgt gcaagatatt atgatgatca ttactgcctt	1080
gactactggg gccaaggcac cacgggcacc gtctcctcag gcgaaggtag tagtactgggt	1140
tctgggtggaa gtggagggttc aggtggagca gacgacattg tactgaccca gtctccagca	1200
actctgtctc tgtctccagg ggagcgtgcc accctgagct gcagagccag tcaaagtgt	1260
agttacatga actggtacca gcagaagccg ggcaaggcac ccaaagatg gatttatgac	1320
acatccaaag tggcttctgg agtccctgct cgcttcagtg gcagtgggtc tgggaccgac	1380
tactctctca caatcaacag cttggaggct gaagatgctg ccacttatta ctgccaacag	1440
tggagtagta acccgctcac gttcggtggc gggaccaagg tggagatcaa a	1491

<210> 269

<211> 497

<212> PRT

<213> artificial sequence

<220>

<223> 5-10/VH7VL2 HLHL

<400> 269

Glu	Val	Gln	Leu	Leu	Glu	Gln	Ser	Gly	Ala	Glu	Leu	Val	Arg	Pro	Gly
1				5					10					15	

Thr	Ser	Val	Lys	Ile	Ser	Cys	Lys	Ala	Ser	Gly	Tyr	Ala	Phe	Thr	Asn
			20					25					30		

Tyr	Trp	Leu	Gly	Trp	Val	Lys	Gln	Arg	Pro	Gly	His	Gly	Leu	Glu	Trp
		35					40					45			

Ile	Gly	Asp	Ile	Phe	Pro	Gly	Ser	Gly	Asn	Ile	His	Tyr	Asn	Glu	Lys
	50					55					60				

Phe	Lys	Gly	Lys	Ala	Thr	Leu	Thr	Ala	Asp	Lys	Ser	Ser	Ser	Thr	Ala
65					70					75				80	

Tyr	Met	Gln	Leu	Ser	Ser	Leu	Thr	Phe	Glu	Asp	Ser	Ala	Val	Tyr	Phe
				85					90					95	

Cys	Ala	Arg	Leu	Arg	Asn	Trp	Asp	Glu	Pro	Met	Asp	Tyr	Trp	Gly	Gln
			100					105					110		

Gly	Thr	Thr	Val	Thr	Val	Ser	Ser	Gly	Gly	Gly	Gly	Ser	Gly	Gly	Gly
			115				120					125			

Gly Ser Gly Gly Gly Gly Ser Glu Leu Val Met Thr Gln Ser Pro Ser
 130 135 140
 Ser Leu Thr Val Thr Ala Gly Glu Lys Val Thr Met Ser Cys Lys Ser
 145 150 155 160
 Ser Gln Ser Leu Leu Asn Ser Gly Asn Gln Lys Asn Tyr Leu Thr Trp
 165 170 175
 Tyr Gln Gln Lys Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr Trp Ala
 180 185 190
 Ser Thr Arg Glu Ser Gly Val Pro Asp Arg Phe Thr Gly Ser Gly Ser
 195 200 205
 Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Val Gln Ala Glu Asp Leu
 210 215 220
 Ala Val Tyr Tyr Cys Gln Asn Asp Tyr Ser Tyr Pro Leu Thr Phe Gly
 225 230 235 240
 Ala Gly Thr Lys Leu Glu Ile Lys Ser Gly Gly Gly Gly Ser Asp Val
 245 250 255
 Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val
 260 265 270
 Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met
 275 280 285
 His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr
 290 295 300
 Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe Lys Asp
 305 310 315 320
 Arg Val Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu
 325 330 335
 Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg
 340 345 350
 Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr
 355 360 365
 Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly Gly Ser
 370 375 380
 Gly Gly Ser Gly Gly Ala Asp Asp Ile Val Leu Thr Gln Ser Pro Ala
 385 390 395 400

Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala
 405 410 415

Ser Gln Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro Gly Lys
 420 425 430

Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser Gly Val
 435 440 445

Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr
 450 455 460

Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys Gln Gln
 465 470 475 480

Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile
 485 490 495

Lys

<210> 270

<211> 1488

<212> DNA

<213> artificial sequence

<220>

<223> 5-10/VL2VH7 LHLH

<400> 270
 gagctcgtga tgacacagtc tccatcctcc ctgactgtga cagcaggaga gaaggctcact 60
 atgagctgca agtccagtca gagtctgtta aacagtggaa atcaaaagaa ctacttgacc 120
 tgggtaccagc agaaaccagg gcagcctcct aaactgttga tctactgggc atccactagg 180
 gaatctgggg tccctgatcg cttcacaggc agtggatctg gaacagattt cactctcacc 240
 atcagcagtg tgcaggctga agacctggca gtttattact gtcagaatga ttatagttat 300
 ccgctcacgt tcggtgctgg gaccaagctt gagatcaaag gtggtggtgg ttctggcggc 360
 ggcggctccg gtggtggtgg ttctgagggtg cagctgctcg agcagtctgg agctgagctg 420
 gtaaggcctg ggacttcagt gaagatatcc tgcaaggcct ctggatacgc cttcactaac 480
 tactggctag gttgggtaaa gcagaggcct ggacatggac ttgagtggat tggagatatt 540
 ttccctggaa gtggtaatat ccactacaat gagaagttca agggcaaagc cacactgact 600
 gcagacaaat cttcgagcac agcctatatg cagctcagta gcctgacatt tgaggactct 660
 gctgtctatt tctgtgcaag actgaggaac tgggacgagc ctatggacta ctggggccaa 720
 gggaccacgg tcaccgtctc ctccggaggt ggtggatccg acattgtact gaccagctct 780

ccagcaactc tgtctctgtc tccaggggag cgtgccaccc tgagctgcag agccagtcaa 840
 agtgtaagtt acatgaactg gtaccagcag aagccgggca aggcacccaa aagatggatt 900
 tatgacacat ccaaagtggc ttctggagtc cctgctcgct tcagtggcag tgggtctggg 960
 accgactact ctctcacaat caacagcttg gaggtgaag atgctgccac ttattactgc 1020
 caacagtgga gtagtaaccc gctcacgttc ggtggcggga ccaaggtgga gatcaaaggc 1080
 gaaggtacta gtactgggtc tgggtggaagt ggaggttcag gtggagcaga cgacgtccaa 1140
 ctggtgcagt caggggctga agtgaaaaaa cctggggcct cagtgaaggt gtcctgcaag 1200
 gcttctggct acacctttac taggtacacg atgcactggg taaggcaggc acctggacag 1260
 ggtctggaat ggattggata cattaatcct agccgtgggt atactaatta caatcagaag 1320
 ttcaaggacc gcgtcacaat cactacagac aaatccacca gcacagccta catggaactg 1380
 agcagcctgc gttctgagga cactgcagtc tattactgtg caagatatta tgatgatcat 1440
 tactgccttg actactgggg ccaaggcacc acggtcaccg tctcctca 1488

<210> 271

<211> 496

<212> PRT

<213> artificial sequence

<220>

<223> 5-10/VL2VH7 LHLH

<400> 271

Glu Leu Val Met Thr Gln Ser Pro Ser Ser Leu Thr Val Thr Ala Gly
 1 5 10 15

Glu Lys Val Thr Met Ser Cys Lys Ser Ser Gln Ser Leu Leu Asn Ser
 20 25 30

Gly Asn Gln Lys Asn Tyr Leu Thr Trp Tyr Gln Gln Lys Pro Gly Gln
 35 40 45

Pro Pro Lys Leu Leu Ile Tyr Trp Ala Ser Thr Arg Glu Ser Gly Val
 50 55 60

Pro Asp Arg Phe Thr Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
 65 70 75 80

Ile Ser Ser Val Gln Ala Glu Asp Leu Ala Val Tyr Tyr Cys Gln Asn
 85 90 95

Asp Tyr Ser Tyr Pro Leu Thr Phe Gly Ala Gly Thr Lys Leu Glu Ile
 100 105 110

Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Ser
 115 120 125

Glu Val Gln Leu Leu Glu Gln Ser Gly Ala Glu Leu Val Arg Pro Gly
 130 135 140

Thr Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Thr Asn
 145 150 155 160

Tyr Trp Leu Gly Trp Val Lys Gln Arg Pro Gly His Gly Leu Glu Trp
 165 170 175

Ile Gly Asp Ile Phe Pro Gly Ser Gly Asn Ile His Tyr Asn Glu Lys
 180 185 190

Phe Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala
 195 200 205

Tyr Met Gln Leu Ser Ser Leu Thr Phe Glu Asp Ser Ala Val Tyr Phe
 210 215 220

Cys Ala Arg Leu Arg Asn Trp Asp Glu Pro Met Asp Tyr Trp Gly Gln
 225 230 235 240

Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp Ile Val
 245 250 255

Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala
 260 265 270

Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Tyr Met Asn Trp Tyr
 275 280 285

Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser
 290 295 300

Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly
 305 310 315 320

~~Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala~~
 325 330 335

Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly
 340 345 350

Gly Thr Lys Val Glu Ile Lys Gly Glu Gly Thr Ser Thr Gly Ser Gly
 355 360 365

Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Val Gln Leu Val Gln Ser
 370 375 380

Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys
 385 390 395 400

Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp Val Arg Gln
 405 410 415

Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn Pro Ser Arg
 420 425 430

Gly Tyr Thr Asn Tyr Asn Gln Lys Phe Lys Asp Arg Val Thr Ile Thr
 435 440 445

Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg
 450 455 460

Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Tyr Tyr Asp Asp His
 465 470 475 480

Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
 485 490 495

<210> 272

<211> 1491

<212> DNA

<213> artificial sequence

<220>

<223> 5-10/VL2VH7 HLLH

<400> 272

gaggtgcagc tgctcgagca gtctggagct gagctggtaa ggcctgggac ttcagtgaag	60
atatcctgca aggcttctgg atacgccttc actaactact ggctagggtg ggtaaagcag	120
aggcctggac atggacttga gtggattgga gatattttcc ctggaagtgg taatatccac	180
tacaatgaga agttcaaggg caaagccaca ctgactgcag acaaatcttc gagcacagcc	240
tatatgcagc tcagtagcct gacatttgag gactctgctg tctatttctg tgcaagactg	300
aggaactggg acgagcctat ggactactgg ggccaagggg ccacggtcac cgtctcctca	360
ggtggtggtg gttctggcgg cggcggctcc ggtggtggtg gttctgagct cgtgatgaca	420
cagtctccat cctccctgac tgtgacagca ggagagaagg tcaactatgag ctgcaagtcc	480
agtcagagtc tgtaaacag tggaaatcaa aagaactact tgacctggta ccagcagaaa	540
ccagggcagc ctctaaact gttgatctac tgggcatcca ctagggaatc tgggggtccct	600
gatcgcttca caggcagtgg atctggaaca gatttcactc tcaccatcag cagtgtgcag	660
gctgaagacc tggcagttta ttactgtcag aatgattata gttatccgct cacgttcggt	720
gctgggacca agcttgagat caaatccgga ggtggtggat ccgacattgt actgaccag	780

244

tctccagcaa ctctgtctct gtctccaggg gagcgtgcc	ccctgagctg cagagccagt	840
caaagtgtaa gttacatgaa ctggtaccag cagaagccgg	gcaaggcacc caaaagatgg	900
atztatgaca catccaaagt ggcttctgga gtccctgctc	gcttcagtgg cagtgggtct	960
gggaccgact actctctcac aatcaacagc ttggaggctg	aagatgctgc cacttattac	1020
tgccaacagt ggagtagtaa cccgctcacg ttcggtggcg	ggaccaaggt ggagatcaaa	1080
ggcgaaggta ctagtactgg ttctggtgga agtggaggtt	caggtggagc agacgacgtc	1140
caactggtgc agtcagggggc tgaagtga aaacctgggg	cctcagtga ggtgtcctgc	1200
aaggcttctg gctacacctt tactaggtac acgatgcact	gggtaaggca ggcacctgga	1260
cagggctctgg aatggattgg atacattaat cctagccgtg	gttatactaa ttacaatcag	1320
aagttcaagg accgcgtcac aatcactaca gacaaatcca	ccagcacagc ctacatggaa	1380
ctgagcagcc tgcgttctga ggacactgca gtctattact	gtgcaagata ttatgatgat	1440
cattactgcc ttgactactg gggccaaggc accacggtca	ccgtctcctc a	1491

<210> 273

<211> 497

<212> PRT

<213> artificial sequence

<220>

<223> 5-10/VL2VH7 HLLH

<400> 273

Glu Val Gln Leu Leu Glu Gln Ser Gly Ala Glu Leu Val Arg Pro Gly
1 5 10 15

Thr Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Thr Asn
20 25 30

Tyr Trp Leu Gly Trp Val Lys Gln Arg Pro Gly His Gly Leu Glu Trp
35 40 45

Ile Gly Asp Ile Phe Pro Gly Ser Gly Asn Ile His Tyr Asn Glu Lys
50 55 60

Phe Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala
65 70 75 80

Tyr Met Gln Leu Ser Ser Leu Thr Phe Glu Asp Ser Ala Val Tyr Phe
85 90 95

Cys Ala Arg Leu Arg Asn Trp Asp Glu Pro Met Asp Tyr Trp Gly Gln
100 105 110

Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Gly Ser Gly Gly Gly
 115 120 245 125

Gly Ser Gly Gly Gly Gly Ser Glu Leu Val Met Thr Gln Ser Pro Ser
 130 135 140

Ser Leu Thr Val Thr Ala Gly Glu Lys Val Thr Met Ser Cys Lys Ser
 145 150 155 160

Ser Gln Ser Leu Leu Asn Ser Gly Asn Gln Lys Asn Tyr Leu Thr Trp
 165 170 175

Tyr Gln Gln Lys Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr Trp Ala
 180 185 190

Ser Thr Arg Glu Ser Gly Val Pro Asp Arg Phe Thr Gly Ser Gly Ser
 195 200 205

Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Val Gln Ala Glu Asp Leu
 210 215 220

Ala Val Tyr Tyr Cys Gln Asn Asp Tyr Ser Tyr Pro Leu Thr Phe Gly
 225 230 235 240

Ala Gly Thr Lys Leu Glu Ile Lys Ser Gly Gly Gly Gly Ser Asp Ile
 245 250 255

Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg
 260 265 270

Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Tyr Met Asn Trp
 275 280 285

Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr
 290 295 300

Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser
 305 310 315 320

Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala
 325 330 335

Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly
 340 345 350

Gly Gly Thr Lys Val Glu Ile Lys Gly Glu Gly Thr Ser Thr Gly Ser
 355 360 365

Gly Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Val Gln Leu Val Gln
 370 375 380

Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys

**385 390 246
 395 400**

Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn Pro Ser
420 425 430

Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser Ser Leu
450 455 460

His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser
485 490 495

<210> 274

<220>

<400> 274

gggaccacgg tcaccgtctc ctccggaggt ggtggatccg acgtccaact ggtgcagtca 780
 ggggctgaag tgaaaaaacc tggggcctca gtgaagggtgt cctgcaaggc ttctggctac 840
 acctttacta ggtacacgat gcactgggta aggcaggcac ctggacaggg tctggaatgg 900
 attggataca ttaatcctag ccgtgggttat actaattaca atcagaagtt caaggaccgc 960
 gtcacaatca ctacagacaa atccaccagc acagcctaca tggaactgag cagcctgcgt 1020
 tctgaggaca ctgcagtcta ttactgtgca agatattatg atgatcatta ctgccttgac 1080
 tactggggcc aaggcaccac ggtcaccgtc tcctcaggcg aaggtagtag tactgggttct 1140
 ggtggaagtg gaggttcagg tggagcagac gacattgtac tgaccagtc tccagcaact 1200
 ctgtctctgt ctccagggga gcgtgccacc ctgacctgca gagccagttc aagtgttaagt 1260
 tacatgaact ggtaccagca gaagccgggc aaggcaccca aaagatggat ttatgacaca 1320
 tccaaagtgg cttctggagt ccctgctcgc ttcagtggca gtgggtctgg gaccgactac 1380
 tctctcacia tcaacagctt ggaggctgaa gatgctgcca cttattactg ccaacagtgg 1440
 agtagtaacc cgctcacgtt cggtggcggg accaaggtgg agatcaaa 1488

<210> 275

<211> 496

<212> PRT

<213> artificial sequence

<220>

<223> 5-10/VH7VL3 LHHL

<400> 275

Glu Leu Val Met Thr Gln Ser Pro Ser Ser Leu Thr Val Thr Ala Gly
 1 5 10 15

Glu Lys Val Thr Met Ser Cys Lys Ser Ser Gln Ser Leu Leu Asn Ser
 20 25 30

Gly Asn Gln Lys Asn Tyr Leu Thr Trp Tyr Gln Gln Lys Pro Gly Gln
 35 40 45

Pro Pro Lys Leu Leu Ile Tyr Trp Ala Ser Thr Arg Glu Ser Gly Val
 50 55 60

Pro Asp Arg Phe Thr Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
 65 70 75 80

Ile Ser Ser Val Gln Ala Glu Asp Leu Ala Val Tyr Tyr Cys Gln Asn
 85 90 95

Asp Tyr Ser Tyr Pro Leu Thr Phe Gly Ala Gly Thr Lys Leu Glu Ile

100	105	248	110
Lys Gly Gly Gly Gly ser Gly Gly Gly Gly ser Gly Gly Gly Gly ser			
115	120	125	
Glu Val Gln Leu Leu Glu Gln ser Gly Ala Glu Leu Val Arg Pro Gly			
130	135	140	
Thr ser Val Lys Ile ser Cys Lys Ala ser Gly Tyr Ala Phe Thr Asn			
145	150	155	160
Tyr Trp Leu Gly Trp Val Lys Gln Arg Pro Gly His Gly Leu Glu Trp			
	165	170	175
Ile Gly Asp Ile Phe Pro Gly ser Gly Asn Ile His Tyr Asn Glu Lys			
	180	185	190
Phe Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys ser ser ser Thr Ala			
	195	200	205
Tyr Met Gln Leu ser ser Leu Thr Phe Glu Asp ser Ala Val Tyr Phe			
	210	215	220
Cys Ala Arg Leu Arg Asn Trp Asp Glu Pro Met Asp Tyr Trp Gly Gln			
225	230	235	240
Gly Thr Thr Val Thr Val ser ser Gly Gly Gly Gly ser Asp Val Gln			
	245	250	255
Leu Val Gln ser Gly Ala Glu Val Lys Lys Pro Gly Ala ser Val Lys			
	260	265	270
Val ser Cys Lys Ala ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His			
	275	280	285
Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile			
	290	295	300
Asn Pro ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe Lys Asp Arg			
305	310	315	320
Val Thr Ile Thr Thr Asp Lys ser Thr ser Thr Ala Tyr Met Glu Leu			
	325	330	335
ser ser Leu Arg ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Tyr			
	340	345	350
Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val			
	355	360	365
Thr Val ser ser Gly Glu Gly Thr ser Thr Gly ser Gly Gly ser Gly			
	370	375	380

Gly Ser Gly Gly Ala Asp Asp Ile Val Leu Thr Gln Ser Pro Ala Thr
385 390 395 400

Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Thr Cys Arg Ala Ser
405 410 415

Ser Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala
420 425 430

Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser Gly Val Pro
435 440 445

Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile
450 455 460

Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp
465 470 475 480

Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
485 490 495

<210> 276

<211> 1491

<212> DNA

<213> artificial sequence

<220>

<223> 5-10/VH7VL3 HLHL

<400> 276

gaggtgcagc tgctcgagca gtctggagct gagctggtaa ggcctgggac ttcagtgaag	60
atatcctgca aggcttctgg atacgccttc actaactact ggctaggttg ggtaaagcag	120
aggcctggac atggacttga gtggattgga gatattttcc ctggaagtgg taatatccac	180
tacaatgaga agttcaaggg caaagccaca ctgactgcag acaaatcttc gagcacagcc	240
tatatgcagc tcagtagcct gacatttgag gactctgctg tctatttctg tgcaagactg	300
aggaactggg acgagcctat ggactactgg ggccaaggga ccacggtcac cgtctcctca	360
ggtggtggtg gttctggcgg cggcggctcc ggtggtggtg gttctgagct cgtgatgaca	420
cagtctccat cctccctgac tgtgacagca ggagagaagg tcactatgag ctgcaagtcc	480
agtcagagtc tgttaaacag tggaaatcaa aagaactact tgacctggta ccagcagaaa	540
ccagggcagc ctccctaaact gttgatctac tgggcatcca ctagggaatc tggggtcctt	600
gatcgcttca caggcagtgg atctggaaca gatttcactc tcaccatcag cagtgtgcag	660
gctgaagacc tggcagttta ttactgtcag aatgattata gttatccgct cacgttcggt	720

250

gctgggacca agcttgagat caaatccgga ggtggtggat ccgacgtcca actggtgcag	780
tcaggggctg aagtgaaaaa acctggggcc tcagtgaagg tgtcctgcaa ggcttctggc	840
tacaccttta ctaggtacac gatgcactgg gtaaggcagg cacctggaca gggctctggaa	900
tggattggat acattaatcc tagccgtggt tatactaatt acaatcagaa gttcaaggac	960
cgcgtcacia tcactacaga caaatccacc agcacagcct acatggaact gagcagcctg	1020
cgttctgagg acactgcagt ctattactgt gcaagatatt atgatgatca ttactgcctt	1080
gactactggg gccaaggcac cacggtcacc gtctcctcag gcgaagggtac tagtactggt	1140
tctggtggaa gtggagggttc aggtggagca gacgacattg tactgacca gtctccagca	1200
actctgtctc tgtctccagg ggagcgtgcc accctgacct gcagagccag ttcaagtgt	1260
agttacatga actggtacca gcagaagccg ggcaaggcac ccaaaagatg gatttatgac	1320
acatccaaag tggcttctgg agtccctgct cgcttcagtg gcagtgggtc tgggaccgac	1380
tactctctca caatcaacag cttggaggct gaagatgctg ccacttatta ctgccaacag	1440
tggagtagta acccgctcac gttcgggtggc gggaccaagg tggagatcaa a	1491

<210> 277

<211> 497

<212> PRT

<213> artificial sequence

<220>

<223> 5-10/VH7VL3 HLHL

<400> 277

Glu Val Gln Leu Leu Glu Gln Ser Gly Ala Glu Leu Val Arg Pro Gly
1 5 10 15

Thr Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Thr Asn
20 25 30

Tyr Trp Leu Gly Trp Val Lys Gln Arg Pro Gly His Gly Leu Glu Trp
35 40 45

Ile Gly Asp Ile Phe Pro Gly Ser Gly Asn Ile His Tyr Asn Glu Lys
50 55 60

Phe Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala
65 70 75 80

Tyr Met Gln Leu Ser Ser Leu Thr Phe Glu Asp Ser Ala Val Tyr Phe
85 90 95

Cys Ala Arg Leu Arg Asn Trp Asp Glu Pro Met Asp Tyr Trp Gly Gln
100 105 110

Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly
 115 120 125
 Gly Ser Gly Gly Gly Gly Ser Glu Leu Val Met Thr Gln Ser Pro Ser
 130 135 140
 Ser Leu Thr Val Thr Ala Gly Glu Lys Val Thr Met Ser Cys Lys Ser
 145 150 155 160
 Ser Gln Ser Leu Leu Asn Ser Gly Asn Gln Lys Asn Tyr Leu Thr Trp
 165 170 175
 Tyr Gln Gln Lys Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr Trp Ala
 180 185 190
 Ser Thr Arg Glu Ser Gly Val Pro Asp Arg Phe Thr Gly Ser Gly Ser
 195 200 205
 Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Val Gln Ala Glu Asp Leu
 210 215 220
 Ala Val Tyr Tyr Cys Gln Asn Asp Tyr Ser Tyr Pro Leu Thr Phe Gly
 225 230 235 240
 Ala Gly Thr Lys Leu Glu Ile Lys Ser Gly Gly Gly Gly Ser Asp Val
 245 250 255
 Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val
 260 265 270
 Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met
 275 280 285
 His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr
 290 295 300
 Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe Lys Asp
 305 310 315 320
 Arg Val Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu
 325 330 335
 Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg
 340 345 350
 Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr
 355 360 365
 Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly Gly Ser
 370 375 380

Gly Gly Ser Gly Gly Ala Asp Asp Ile Val Leu Thr Gln Ser Pro Ala
385 390 395 400

Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Thr Cys Arg Ala
405 410 415

Ser Ser Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro Gly Lys
420 425 430

Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser Gly Val
435 440 445

Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr
450 455 460

Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys Gln Gln
465 470 475 480

Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile
485 490 495

Lys

<210> 278

<211> 1488

<212> DNA

<213> artificial sequence

<220>

<223> 5-10/VL3VH7 LHLH

<400> 278
gagctcgtga tgacacagtc tccatcctcc ctgactgtga cagcaggaga gaaggtcact 60
atgagctgca agtccagtc gagtctgtta aacagtggaa atcaaaagaa ctacttgacc 120
tggtaccagc agaaaccagg gcagcctcct aaactgttga tctactgggc atccactagg 180
gaatctgggg tccctgatcg cttcacaggc agtggatctg gaacagattt cactctcacc 240
atcagcagtg tgcaggctga agacctggca gtttattact gtcagaatga ttatagttat 300
ccgctcacgt tcggtgctgg gaccaagctt gagatcaaag gtggtggtgg ttctggcggc 360
ggcggctccg gtggtggtgg ttctgaggtg cagctgctcg agcagtctgg agctgagctg 420
gtaaggcctg ggacttcagt gaagatatcc tgcaaggctt ctggatacgc cttcactaac 480
tactggctag gttgggtaaa gcagaggcct ggacatggac ttgagtggat tggagatatt 540
ttccctggaa gtggtaatat ccactacaat gagaagttca agggcaaagc cacactgact 600
gcagacaaat cttcgagcac agcctatatg cagctcagta gcctgacatt tgaggactct 660

gctgtctatt tctgtgcaag actgaggaac tgggacgagc ctatggacta ctggggccaa 720
 gggaccacgg tcaccgtctc ctccggaggt ggtggatccg acattgtact gacccagtct 780
 ccagcaactc tgtctctgtc tccaggggag cgtgccaccc tgacctgcag agccagttca 840
 agtgtaagtt acatgaactg gtaccagcag aagccgggca aggcacccaa aagatggatt 900
 tatgacacat ccaaagtggc ttctggagtc cctgctcgct tcagtggcag tgggtctggg 960
 accgactact ctctcacaat caacagcttg gaggctgaag atgctgccac ttattactgc 1020
 caacagtgga gtagtaaccc gctcacgttc ggtggcggga ccaaggtgga gatcaaaggc 1080
 gaaggacta gtactgggtc tgggtggaagt ggaggttcag gtggagcaga cgacgtccaa 1140
 ctggtgcagt caggggctga agtgaaaaaa cctggggcct cagtgaagggt gtcctgcaag 1200
 gcttctggct acacctttac taggtacacg atgcactggg taaggcaggc acctggacag 1260
 ggtctggaat ggattggata cattaatcct agccgtgggt atactaatta caatcagaag 1320
 ttcaaggacc gcgtcacaat cactacagac aaatccacca gcacagccta catggaactg 1380
 agcagcctgc gttctgagga cactgcagtc tattactgtg caagatatta tgatgatcat 1440
 tactgccttg actactgggg ccaaggcacc acggtcaccg tctcctca 1488

<210> 279

<211> 496

<212> PRT

<213> artificial sequence

<220>

<223> 5-10/VL3VH7 LHLH

<400> 279

Glu Leu Val Met Thr Gln Ser Pro Ser Ser Leu Thr Val Thr Ala Gly
 1 5 10 15

Glu Lys Val Thr Met Ser Cys Lys Ser Ser Gln Ser Leu Leu Asn Ser
 20 25 30

Gly Asn Gln Lys Asn Tyr Leu Thr Trp Tyr Gln Gln Lys Pro Gly Gln
 35 40 45

Pro Pro Lys Leu Leu Ile Tyr Trp Ala Ser Thr Arg Glu Ser Gly Val
 50 55 60

Pro Asp Arg Phe Thr Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
 65 70 75 80

Ile Ser Ser Val Gln Ala Glu Asp Leu Ala Val Tyr Tyr Cys Gln Asn
 85 90 95

Asp Tyr Ser Tyr Pro Leu Thr Phe Gly Ala Gly Thr Lys Leu Glu Ile
 100 105 110

Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Ser
 115 120 125

Glu Val Gln Leu Leu Glu Gln Ser Gly Ala Glu Leu Val Arg Pro Gly
 130 135 140

Thr Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Thr Asn
 145 150 155 160

Tyr Trp Leu Gly Trp Val Lys Gln Arg Pro Gly His Gly Leu Glu Trp
 165 170 175

Ile Gly Asp Ile Phe Pro Gly Ser Gly Asn Ile His Tyr Asn Glu Lys
 180 185 190

Phe Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala
 195 200 205

Tyr Met Gln Leu Ser Ser Leu Thr Phe Glu Asp Ser Ala Val Tyr Phe
 210 215 220

Cys Ala Arg Leu Arg Asn Trp Asp Glu Pro Met Asp Tyr Trp Gly Gln
 225 230 235 240

Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp Ile Val
 245 250 255

Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala
 260 265 270

Thr Leu Thr Cys Arg Ala Ser Ser Ser Val Ser Tyr Met Asn Trp Tyr
 275 280 285

Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser
 290 295 300

~~Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly~~
 305 310 315 320

Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala
 325 330 335

Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly
 340 345 350

Gly Thr Lys Val Glu Ile Lys Gly Glu Gly Thr Ser Thr Gly Ser Gly
 355 360 365

Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Val²⁵⁵ Gln Leu Val Gln Ser
370 375 380

Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys
385 390 395 400

Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp Val Arg Gln
405 410 415

Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn Pro Ser Arg
420 425 430

Gly Tyr Thr Asn Tyr Asn Gln Lys Phe Lys Asp Arg Val Thr Ile Thr
435 440 445

Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg
450 455 460

Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Tyr Tyr Asp Asp His
465 470 475 480

Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
485 490 495

<210> 280

<211> 1491

<212> DNA

<213> artificial sequence

<220>

<223> 5-10/VL3VH7 HLLH

<400> 280

gaggtgcagc tgctcgagca gtctggagct gagctggtaa ggcctgggac ttcagtgaag	60
atatcctgca aggcttctgg atacgccttc actaactact ggctaggttg ggtaaagcag	120
aggcctggac atggacttga gtggattgga gatattttcc ctggaagtgg taatatccac	180
tacaatgaga agttcaaggg caaagccaca ctgactgcag acaaactctc gagcacagcc	240
tatatgcagc tcagtagcct gacatttgag gactctgctg tctatttctg tgcaagactg	300
aggaactggg acgagcctat ggactactgg ggccaaggga ccacggtcac cgtctcctca	360
ggtggtggtg gttctggcgg cggcggctcc ggtggtggtg gttctgagct cgtgatgaca	420
cagtctccat cctccctgac tgtgacagca ggagagaagg tcactatgag ctgcaagtcc	480
agtcagagtc tgttaaacag tggaatatcaa aagaactact tgacctggta ccagcagaaa	540
ccagggcagc ctctaaact gttgatctac tgggcatcca ctagggaatc tgggggtccct	600
gatcgcttca caggcagtgg atctggaaca gatttcactc tcaccatcag cagtgtgcag	660

256

gctgaagacc tggcagttta ttactgtcag aatgattata gttatccgct cacgttcggt	720
gctgggacca agcttgagat caaatccgga ggtggtggat ccgacattgt actgacccag	780
tctccagcaa ctctgtctct gtctccaggg gagcgtgcca ccctgacctg cagagccagt	840
tcaagtgtaa gttacatgaa ctggtaccag cagaagccgg gcaaggcacc caaaagatgg	900
atztatgaca catccaaagt ggcttctgga gtccctgctc gcttcagtgg cagtgggtct	960
gggaccgact actctctcac aatcaacagc ttggaggctg aagatgctgc cacttattac	1020
tgccaacagt ggagtagtaa cccgctcacg ttcggtggcg ggaccaaggt ggagatcaaa	1080
ggcgaaggta ctagtactgg ttctggtgga agtggagggt cagggtggagc agacgacgtc	1140
caactggtgc agtcagggggc tgaagtgaaa aaacctgggg cctcagtgaa ggtgtcctgc	1200
aaggcttctg gctacacctt tactaggtac acgatgcact gggtaaggca ggcacctgga	1260
cagggtctgg aatggattgg atacattaat cctagccgtg gttatactaa ttacaatcag	1320
aagttcaagg accgcgtcac aatcactaca gacaaatcca ccagcacagc ctacatggaa	1380
ctgagcagcc tgcgttctga ggacactgca gtctattact gtgcaagata ttatgatgat	1440
cattactgcc ttgactactg gggccaaggc accacgggtca ccgtctcctc a	1491

<210> 281

<211> 497

<212> PRT

<213> artificial sequence

<220>

<223> 5-10/VL3VH7 HLLH

<400> 281

Glu	Val	Gln	Leu	Leu	Glu	Gln	Ser	Gly	Ala	Glu	Leu	Val	Arg	Pro	Gly
1			5					10					15		

Thr	Ser	Val	Lys	Ile	Ser	Cys	Lys	Ala	Ser	Gly	Tyr	Ala	Phe	Thr	Asn
			20					25					30		

Tyr	Trp	Leu	Gly	Trp	Val	Lys	Gln	Arg	Pro	Gly	His	Gly	Leu	Glu	Trp
		35				40					45				

Ile	Gly	Asp	Ile	Phe	Pro	Gly	Ser	Gly	Asn	Ile	His	Tyr	Asn	Glu	Lys
	50					55				60					

Phe	Lys	Gly	Lys	Ala	Thr	Leu	Thr	Ala	Asp	Lys	Ser	Ser	Ser	Thr	Ala
65					70					75					80

Tyr	Met	Gln	Leu	Ser	Ser	Leu	Thr	Phe	Glu	Asp	Ser	Ala	Val	Tyr	Phe
			85						90					95	

Cys Ala Arg Leu Arg Asn Trp Asp Glu Pro Met Asp Tyr Trp Gly Gln
 100 105 257 110

Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly
 115 120 125

Gly Ser Gly Gly Gly Gly Ser Glu Leu Val Met Thr Gln Ser Pro Ser
 130 135 140

Ser Leu Thr Val Thr Ala Gly Glu Lys Val Thr Met Ser Cys Lys Ser
 145 150 155 160

Ser Gln Ser Leu Leu Asn Ser Gly Asn Gln Lys Asn Tyr Leu Thr Trp
 165 170 175

Tyr Gln Gln Lys Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr Trp Ala
 180 185 190

Ser Thr Arg Glu Ser Gly Val Pro Asp Arg Phe Thr Gly Ser Gly Ser
 195 200 205

Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Val Gln Ala Glu Asp Leu
 210 215 220

Ala Val Tyr Tyr Cys Gln Asn Asp Tyr Ser Tyr Pro Leu Thr Phe Gly
 225 230 235 240

Ala Gly Thr Lys Leu Glu Ile Lys Ser Gly Gly Gly Gly Ser Asp Ile
 245 250 255

Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg
 260 265 270

Ala Thr Leu Thr Cys Arg Ala Ser Ser Ser Val Ser Tyr Met Asn Trp
 275 280 285

Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr
 290 295 300

Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser
 305 310 315 320

Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala
 325 330 335

Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly
 340 345 350

Gly Gly Thr Lys Val Glu Ile Lys Gly Glu Gly Thr Ser Thr Gly Ser
 355 360 365

Gly Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Val Gln Leu Val Gln

370 375 258 380
 Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys
 385 390 395 400
 Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp Val Arg
 405 410 415
 Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn Pro Ser
 420 425 430
 Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe Lys Asp Arg Val Thr Ile
 435 440 445
 Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser Ser Leu
 450 455 460
 Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Tyr Tyr Asp Asp
 465 470 475 480
 His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser
 485 490 495

Ser

<210> 282
 <211> 1497
 <212> DNA
 <213> artificial sequence

<220>

<223> VL1/VH5x4-7 LHHL

<400> 282
 gacattcaga tgaccagtc tccatctagc ctgtctgcat ctgtcgggga ccgtgtcacc 60
 atcacctgca gagccagtc aagtgtagt tacatgaact ggtaccagca gaagccgggc 120
 aaggcaccca aaagatggat ttatgacaca tccaaagtgg cttctggagt ccctgctcgc 180
 ttcagtggca gtgggtctgg gaccgactac tctctcaca tcaacagctt ggaggctgaa 240
 gatgctgcca cttattactg ccaacagtgg agtagtaacc cgctcacgtt cggtggcggg 300
 accaaggtgg agatcaaagg cgaaggtact agtactgggt ctggtggaag tggaggttca 360
 ggtggagcag acgacgtcca actggtgcag tcaggggctg aagtgaaaaa acctggggcc 420
 tcagtgaagg tgtcctgcaa ggcttctggc tacaccttta ctaggtacac gatgcactgg 480
 gtaaggcagg cacctggaca gggctctggaa tggattggat acattaatcc tagccgtggt 540
 tatactaatt acgcagacag cgtcaagggc cgcttcacaa tcactacaga caaatccacc 600

agcacagcct acatggaact gagcagcctg cgttctgagg acactgcaac ctattactgt 660
 gcaagatatt atgatgatca ttactgcctt gactactggg gccaaaggcac cacgggtcacc 720
 gtctcctccg gaggtggtgg atccgaggtg cagctgctcg agcagtctgg agctgagctg 780
 gcgaggcctg gggcttcagt gaagctgtcc tgcaaggctt ctggctacac cttcaciaaac 840
 tatggtttaa gctgggtgaa gcagaggcct ggacagggtcc ttgagtggat tggagaggtt 900
 taccctagaa ttggtaatgc ttactacaat gagaagttca agggcaaggc cacactgact 960
 gcagacaaat cctccagcac agcgtccatg gagctccgca gcctgacctc tgaggactct 1020
 gcggtctatt tctgtgcaag acgggggatcc tacgatacta actacgactg gtacttcgat 1080
 gtctggggcc aagggaccac ggtcaccgtc tcctcaggtg gtggtggttc tggcggcggc 1140
 ggctccggtg gtggtggttc tgagctcgtg atgaccaga ctccactctc cctgcctgtc 1200
 agtcttgag atcaagcctc catctcttgc agatctagtc agagccttgt acacagtaat 1260
 ggaaacacct atttacattg gtacctgcag aagccaggcc agtctccaaa gctcctgac 1320
 taaaagttt ccaaccgatt ttctggggtc ccagacaggt tcagtggcag tggatcaggg 1380
 acagatttca cactcaagat cagcagagtg gaggtgagg atctgggagt ttatttctgc 1440
 tctcaaagta cacatgttcc gtacacgttc ggagggggga ccaagcttga gatcaaa 1497

<210> 283

<211> 499

<212> PRT

<213> artificial sequence

<220>

<223> VL1/VH5x4-7 LHHL

<400> 283

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Ser Tyr Met
20 25 30

Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr
35 40 45

Asp Thr Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
50 55 60

Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu
65 70 75 80

Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr

85 90 260 95
 Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Gly Glu Gly Thr Ser Thr
 100 105 110
 Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Val Gln Leu
 115 120 125
 Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val
 130 135 140
 Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp
 145 150 155 160
 Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn
 165 170 175
 Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val Lys Gly Arg Phe
 180 185 190
 Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser
 195 200 205
 Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys Ala Arg Tyr Tyr
 210 215 220
 Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr
 225 230 235 240
 Val Ser Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Leu Glu Gln Ser
 245 250 255
 Gly Ala Glu Leu Ala Arg Pro Gly Ala Ser Val Lys Leu Ser Cys Lys
 260 265 270
 Ala Ser Gly Tyr Thr Phe Thr Asn Tyr Gly Leu Ser Trp Val Lys Gln
 275 280 285
 Arg Pro Gly Gln Val Leu Glu Trp Ile Gly Glu Val Tyr Pro Arg Ile
 290 295 300
 Gly Asn Ala Tyr Tyr Asn Glu Lys Phe Lys Gly Lys Ala Thr Leu Thr
 305 310 315 320
 Ala Asp Lys Ser Ser Ser Thr Ala Ser Met Glu Leu Arg Ser Leu Thr
 325 330 335
 Ser Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg Arg Gly Ser Tyr Asp
 340 345 350
 Thr Asn Tyr Asp Trp Tyr Phe Asp Val Trp Gly Gln Gly Thr Thr Val
 355 360 365

Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
370 375 380

Gly Gly Ser Glu Leu Val Met Thr Gln Thr Pro Leu Ser Leu Pro Val
385 390 395 400

Ser Leu Gly Asp Gln Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu
405 410 415

Val His Ser Asn Gly Asn Thr Tyr Leu His Trp Tyr Leu Gln Lys Pro
420 425 430

Gly Gln Ser Pro Lys Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser
435 440 445

Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr
450 455 460

Leu Lys Ile Ser Arg Val Glu Ala Glu Asp Leu Gly Val Tyr Phe Cys
465 470 475 480

Ser Gln Ser Thr His Val Pro Tyr Thr Phe Gly Gly Gly Thr Lys Leu
485 490 495

Glu Ile Lys

<210> 284

<211> 1500

<212> DNA

<213> artificial sequence

<220>

<223> VH5/VL1x4-7 HLHL

<400> 284

gacgtccaac tggtgcagtc aggggctgaa gtgaaaaaac ctggggcctc agtgaagggtg	60
tcctgcaagg cttctggcta cacctttact aggtacacga tgcactgggt aaggcaggca	120
cctggacagg gtctggaatg gattggatac attaataccta gccgtgggta tactaattac	180
gcagacagcg tcaagggccg cttcacaatc actacagaca aatccaccag cacagcctac	240
atggaactga gcagcctgcg ttctgaggac actgcaacct attactgtgc aagatattat	300
gatgatcatt actgccttga ctactggggc caaggcacca cggtcaccgt ctcctcaggc	360
gaagg tacta gtactgggtc tggtggaagt ggagggttcag gtggagcaga cgacattcag	420
atgacccagt ctccatctag cctgtctgca tctgtcgggg accgtgtcac catcacctgc	480

262

agagccagtc aaagtgtaag ttacatgaac tgggtaccagc agaagccggg caaggcaccc	540
aaaagatgga tttatgacac atccaaagtg gcttctggag tccctgctcg cttcagtggc	600
agtgggtctg ggaccgacta ctctctcaca atcaacagct tggaggctga agatgctgcc	660
acttattact gccaacagtg gagtagtaac ccgctcacgt tcggtggcgg gaccaaggtg	720
gagatcaaat ccggaggtgg tggatccgag gtgcagctgc tcgagcagtc tggagctgag	780
ctggcgaggc ctggggcttc agtgaagctg tcctgcaagg cttctggcta caccttcaca	840
aactatggtt taagctgggt gaagcagagg cctggacagg tccttgagtg gattggagag	900
gtttatccta gaattggtaa tgcttactac aatgagaagt tcaagggcaa ggccacactg	960
actgcagaca aatcctccag cacagcgtcc atggagctcc gcagcctgac ctctgaggac	1020
tctgcggtct atttctgtgc aagacgggga tcctacgata ctaactacga ctggtacttc	1080
gatgtctggg gccaagggac cacggtcacc gtctcctcag gtggtggtgg ttctggcggc	1140
ggcggctccg gtggtggtgg ttctgagctc gtgatgaccc agactccact ctccctgcct	1200
gtcagtcttg gagatcaagc ctccatctct tgcagatcta gtcagagcct tgtacacagt	1260
aatggaaaca cctatttaca ttggtacctg cagaagccag gccagtctcc aaagctcctg	1320
atctacaaag tttccaaccg attttctggg gtcccagaca ggttcagtgg cagtggatca	1380
gggacagatt tcacactcaa gatcagcaga gtggaggctg aggatctggg agtttatttc	1440
tgctctcaaa gtacacatgt tccgtacacg ttcggagggg ggaccaagct tgagatcaaa	1500

<210> 285

<211> 500

<212> PRT

<213> artificial sequence

<220>

<223> VH5/VL1x4-7 HLHL

<400> 285

Asp	Val	Gln	Leu	Val	Gln	Ser	Gly	Ala	Glu	Val	Lys	Lys	Pro	Gly	Ala
1			5						10					15	

Ser	Val	Lys	Val	Ser	Cys	Lys	Ala	Ser	Gly	Tyr	Thr	Phe	Thr	Arg	Tyr
			20					25					30		

Thr	Met	His	Trp	Val	Arg	Gln	Ala	Pro	Gly	Gln	Gly	Leu	Glu	Trp	Ile
		35					40					45			

Gly	Tyr	Ile	Asn	Pro	Ser	Arg	Gly	Tyr	Thr	Asn	Tyr	Ala	Asp	Ser	Val
	50					55					60				

Lys	Gly	Arg	Phe	Thr	Ile	Thr	Thr	Asp	Lys	Ser	Thr	Ser	Thr	Ala	Tyr
65					70					75					80

Met Glu Leu Ser Ser₈₅ Leu Arg Ser Glu Asp₉₀ Thr Ala Thr Tyr Tyr₉₅ Cys
 Ala Arg Tyr Tyr₁₀₀ Asp Asp His Tyr Cys₁₀₅ Leu Asp Tyr Trp Gly₁₁₀ Gln Gly
 Thr Thr Val₁₁₅ Thr Val Ser Ser Gly₁₂₀ Glu Gly Thr Ser Thr₁₂₅ Gly Ser Gly
 Gly Ser₁₃₀ Gly Gly Ser Gly Gly₁₃₅ Ala Asp Asp Ile Gln₁₄₀ Met Thr Gln Ser
 Pro₁₄₅ Ser Ser Leu Ser Ala₁₅₀ Ser Val Gly Asp Arg₁₅₅ Val Thr Ile Thr Cys₁₆₀
 Arg Ala Ser Gln Ser₁₆₅ Val Ser Tyr Met Asn₁₇₀ Trp Tyr Gln Gln Lys₁₇₅ Pro
 Gly Lys Ala Pro₁₈₀ Lys Arg Trp Ile Tyr₁₈₅ Asp Thr Ser Lys Val₁₉₀ Ala Ser
 Gly Val₁₉₅ Pro Ala Arg Phe Ser Gly₂₀₀ Ser Gly Ser Gly Thr₂₀₅ Asp Tyr Ser
 Leu Thr₂₁₀ Ile Asn Ser Leu Glu₂₁₅ Ala Glu Asp Ala Ala₂₂₀ Thr Tyr Tyr Cys
 Gln₂₂₅ Gln Trp Ser Ser Asn₂₃₀ Pro Leu Thr Phe Gly₂₃₅ Gly Gly Thr Lys Val₂₄₀
 Glu Ile Lys Ser Gly₂₄₅ Gly Gly Gly Ser Glu₂₅₀ Val Gln Leu Leu Glu₂₅₅ Gln
 Ser Gly Ala Glu₂₆₀ Leu Ala Arg Pro Gly₂₆₅ Ala Ser Val Lys Leu₂₇₀ Ser Cys
 Lys Ala Ser₂₇₅ Gly Tyr Thr Phe Thr₂₈₀ Asn Tyr Gly Leu Ser₂₈₅ Trp Val Lys
 Gln Arg₂₉₀ Pro Gly Gln Val Leu₂₉₅ Glu Trp Ile Gly Glu₃₀₀ Val Tyr Pro Arg
 Ile Gly Asn Ala Tyr Tyr₃₁₀ Asn Glu Lys Phe Lys₃₁₅ Gly Lys Ala Thr Leu₃₂₀
 Thr Ala Asp Lys Ser₃₂₅ Ser Ser Thr Ala Ser₃₃₀ Met Glu Leu Arg Ser₃₃₅ Leu
 Thr Ser Glu Asp₃₄₀ Ser Ala Val Tyr Phe₃₄₅ Cys Ala Arg Arg Gly₃₅₀ Ser Tyr

Asp Thr Asn Tyr Asp Trp Tyr Phe Asp Val Trp Gly Gln Gly Thr Thr
355 360 365

Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
370 375 380

Gly Gly Gly Ser Glu Leu Val Met Thr Gln Thr Pro Leu Ser Leu Pro
385 390 395 400

Val Ser Leu Gly Asp Gln Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser
405 410 415

Leu Val His Ser Asn Gly Asn Thr Tyr Leu His Trp Tyr Leu Gln Lys
420 425 430

Pro Gly Gln Ser Pro Lys Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe
435 440 445

Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe
450 455 460

Thr Leu Lys Ile Ser Arg Val Glu Ala Glu Asp Leu Gly Val Tyr Phe
465 470 475 480

Cys Ser Gln Ser Thr His Val Pro Tyr Thr Phe Gly Gly Gly Thr Lys
485 490 495

Leu Glu Ile Lys
500

<210> 286

<211> 1497

<212> DNA

<213> artificial sequence

<220>

<223> VL1/VH5x4-7-LHLH

<400> 286	
gacattcaga tgaccagtc tccatctagc ctgtctgcat ctgtcgggga ccgtgtcacc	60
atcacctgca gagccagtca aagtgttaagt tacatgaact ggtaccagca gaagccgggc	120
aaggcaccca aaagatggat ttatgacaca tccaaagtgg cttctggagt ccctgctcgc	180
ttcagtggca gtgggtctgg gaccgactac tctctcacia tcaacagctt ggaggctgaa	240
gatgctgccca cttattactg ccaacagtgg agtagtaacc cgctcacgtt cggtggcggg	300
accaaggtgg agatcaaagg cgaaggtact agtactgggt ctggtggaag tggaggttca	360
ggtggagcag acgacgtcca actggtgcag tcaggggctg aagtgaataa acctggggcc	420

tcagtgaagg	tgtcctgcaa	ggcttctggc	tacaccttta	ctaggtacac	gatgcactgg	480
gtaaggcagg	cacctggaca	gggtctggaa	tggattggat	acattaatcc	tagccgtggt	540
tatactaatt	acgcagacag	cgtcaagggc	cgcttcacaa	tcactacaga	caaatccacc	600
agcacagcct	acatggaact	gagcagcctg	cgttctgagg	acactgcaac	ctattactgt	660
gcaagatatt	atgatgatca	ttactgcctt	gactactggg	gccaaggcac	cacggtcacc	720
gtctcctccg	gaggtggtgg	atccgagctc	gtgatgaccc	agactccact	ctccctgcct	780
gtcagtcttg	gagatcaagc	ctccatctct	tgcagatcta	gtcagagcct	tgtacacagt	840
aatggaaaca	cctattttaca	ttggtacctg	cagaagccag	gccagtctcc	aaagctcctg	900
atctacaaag	tttccaaccg	attttctggg	gtcccagaca	ggttcagtgg	cagtggatca	960
gggacagatt	tcacactcaa	gatcagcaga	gtggaggctg	aggatctggg	agttttatttc	1020
tgctctcaaa	gtacacatgt	tccgtacacg	ttcggagggg	ggaccaagct	tgagatcaaa	1080
gggtggtggtg	gttctggcgg	cggcggctcc	gggtggtggtg	gttctgaggt	gcagctgctc	1140
gagcagtctg	gagctgagct	ggcgaggcct	ggggcttcag	tgaagctgtc	ctgcaaggct	1200
tctggctaca	ccttcacaaa	ctatgggttta	agctgggtga	agcagaggcc	tggacaggtc	1260
cttgagtgga	ttggagaggt	ttatcctaga	attggtaatg	cttactacaa	tgagaagttc	1320
aagggcaagg	ccacactgac	tgcagacaaa	tcctccagca	cagcgtccat	ggagctccgc	1380
agcctgacct	ctgaggactc	tgcggtctat	ttctgtgcaa	gacggggatc	ctacgatact	1440
aactacgact	ggtacttcga	tgtctggggc	caagggacca	cggtcaccgt	ctcctca	1497

<210> 287

<211> 499

<212> PRT

<213> artificial sequence

<220>

<223> VL1/VH5x4-7 LHLH

<400> 287

Asp	Ile	Gln	Met	Thr	Gln	Ser	Pro	Ser	Ser	Leu	Ser	Ala	Ser	Val	Gly
1				5				10						15	

Asp	Arg	Val	Thr	Ile	Thr	Cys	Arg	Ala	Ser	Gln	Ser	Val	Ser	Tyr	Met
			20					25					30		

Asn	Trp	Tyr	Gln	Gln	Lys	Pro	Gly	Lys	Ala	Pro	Lys	Arg	Trp	Ile	Tyr
		35					40					45			

Asp	Thr	Ser	Lys	Val	Ala	Ser	Gly	Val	Pro	Ala	Arg	Phe	Ser	Gly	Ser
	50					55					60				

Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu
65 70 75 80

Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr
85 90 95

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Gly Glu Gly Thr Ser Thr
100 105 110

Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Val Gln Leu
115 120 125

Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val
130 135 140

Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp
145 150 155 160

Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn
165 170 175

Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val Lys Gly Arg Phe
180 185 190

Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser
195 200 205

Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys Ala Arg Tyr Tyr
210 215 220

Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr
225 230 235 240

Val Ser Ser Gly Gly Gly Gly Ser Glu Leu Val Met Thr Gln Thr Pro
245 250 255

Leu Ser Leu Pro Val Ser Leu Gly Asp Gln Ala Ser Ile Ser Cys Arg
260 265 270

~~Ser Ser Gln Ser Leu Val His Ser Asn Gly Asn Thr Tyr Leu His Trp~~
~~275 280 285~~

Tyr Leu Gln Lys Pro Gly Gln Ser Pro Lys Leu Leu Ile Tyr Lys Val
290 295 300

Ser Asn Arg Phe Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser
305 310 315 320

Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu Asp Leu
325 330 335

Gly Val Tyr Phe Cys Ser Gln Ser Thr His Val Pro Tyr Thr Phe Gly
340 345 267 350

Gly Gly Thr Lys Leu Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly Gly
355 360 365

Gly Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Leu Glu Gln Ser Gly
370 375 380

Ala Glu Leu Ala Arg Pro Gly Ala Ser Val Lys Leu Ser Cys Lys Ala
385 390 395 400

Ser Gly Tyr Thr Phe Thr Asn Tyr Gly Leu Ser Trp Val Lys Gln Arg
405 410 415

Pro Gly Gln Val Leu Glu Trp Ile Gly Glu Val Tyr Pro Arg Ile Gly
420 425 430

Asn Ala Tyr Tyr Asn Glu Lys Phe Lys Gly Lys Ala Thr Leu Thr Ala
435 440 445

Asp Lys Ser Ser Ser Thr Ala Ser Met Glu Leu Arg Ser Leu Thr Ser
450 455 460

Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg Arg Gly Ser Tyr Asp Thr
465 470 475 480

Asn Tyr Asp Trp Tyr Phe Asp Val Trp Gly Gln Gly Thr Thr Val Thr
485 490 495

Val Ser Ser

<210> 288

<211> 1500

<212> DNA

<213> artificial sequence

<220>

<223> VH5/VL1x4-7 HLLH

<400> 288

gacgtccaac tgggtgcagtc aggggctgaa gtgaaaaaac ctggggcctc agtgaagggtg	60
tcctgcaagg cttctggcta cacctttact aggtacacga tgcactgggt aaggcaggca	120
cctggacagg gtctggaatg gattggatac attaataccta gccgtgggtta tactaattac	180
gcagacagcg tcaagggccg cttcacaatc actacagaca aatccaccag cacagcctac	240
atggaactga gcagcctgcg ttctgaggac actgcaacct attactgtgc aagatattat	300

268

gatgatcatt actgccttga ctactggggc caaggcacca cggtcaccgt ctcctcaggc	360
gaaggtacta gtactgggtc tggtggaagt ggaggttcag gtggagcaga cgacattcag	420
atgaccagtc ctccatctag cctgtctgca tctgtcgggg accgtgtcac catcacctgc	480
agagccagtc aaagtgtaag ttacatgaac tggtagcagc agaagccggg caaggcaccc	540
aaaagatgga tttatgacac atccaaagtg gcttctggag tccctgctcg cttcagtggc	600
agtgggtctg ggaccgacta ctctctcaca atcaacagct tggaggctga agatgctgcc	660
acttattact gccaacagtg gagtagtaac ccgctcacgt tcggtggcgg gaccaagggtg	720
gagatcaaat ccggagggtg tggatccgag ctcgtgatga cccagactcc actctccctg	780
cctgtcagtc ttggagatca agcctccatc tcttgcagat ctagtcagag ccttgtagac	840
agtaatggaa acacctatct acattgggtac ctgcagaagc caggccagtc tccaaagctc	900
ctgatctaca aagtttccaa ccgattttct ggggtcccag acagggttcag tggcagtggg	960
tcagggacag atttcacact caagatcagc agagtggagg ctgaggatct gggagtttat	1020
ttctgctctc aaagtacaca tgttccgtac acgttcggag gggggaccaa gcttgagatc	1080
aaagggtggtg gtggttctgg cggcggcggc tccggtggtg gtggttctga ggtgcagctg	1140
ctcgagcagt ctggagctga gctggcgagg cctggggctt cagtgaagct gtcctgcaag	1200
gcttctgggt acaccttcac aaactatggt ttaagctggg tgaagcagag gcctggacag	1260
gtccttgagt ggattggaga ggtttatcct agaattggta atgcttacta caatgagaag	1320
ttcaagggca aggccacact gactgcagac aaatcctcca gcacagcgtc catggagctc	1380
cgcagcctga cctctgagga ctctgcggtc tatttctgtg caagacgggg atcctacgat	1440
actaactacg actggtactt cgatgtctgg ggccaagggg ccacgggtcac cgtctcctca	1500

<210> 289

<211> 500

<212> PRT

<213> artificial sequence

<220>

<223> VH5/VL1x4-7 HLLH

<400> 289

Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr
20 25 30

Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr²⁶⁹ Asn Tyr Ala Asp Ser Val
 50 55 60

Lys Gly Arg Phe Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr
 65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys
 85 90 95

Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
 100 105 110

Thr Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly
 115 120 125

Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Gln Met Thr Gln Ser
 130 135 140

Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys
 145 150 155 160

Arg Ala Ser Gln Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro
 165 170 175

Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser
 180 185 190

Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser
 195 200 205

Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys
 210 215 220

Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
 225 230 235 240

Glu Ile Lys Ser Gly Gly Gly Gly Ser Glu Leu Val Met Thr Gln Thr
 245 250 255

Pro Leu Ser Leu Pro Val Ser Leu Gly Asp Gln Ala Ser Ile Ser Cys
 260 265 270

Arg Ser Ser Gln Ser Leu Val His Ser Asn Gly Asn Thr Tyr Leu His
 275 280 285

Trp Tyr Leu Gln Lys Pro Gly Gln Ser Pro Lys Leu Leu Ile Tyr Lys
 290 295 300

Val Ser Asn Arg Phe Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly
 305 310 315 320

Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu Asp

gatgctgcca	cttattactg	ccaacagtgg	agtagtaacc	cgctcacgtt	cggtggcggg	300
accaaggtgg	agatcaaagg	cgaaggtact	agtactgggt	ctggtggaag	tggaggttca	360
ggtggagcag	acgacgtcca	actggtgcag	tcaggggctg	aagtgaaaaa	acctggggcc	420
tcagtgaagg	tgtcctgcaa	ggcttctggc	tacaccttta	ctaggtacac	gatgcactgg	480
gtaaggcagg	cacctggaca	gggtctggaa	tggattggat	acattaatcc	tagccgtggg	540
tatactaatt	acgcagacag	cgtcaagggc	cgcttcacaa	tcactacaga	caaatccacc	600
agcacagcct	acatggaact	gagcagcctg	cgttctgagg	acactgcaac	ctattactgt	660
gcaagatatt	atgatgatca	ttactgcctt	gactactggg	gccaaggcac	cacggtcacc	720
gtctcctccg	gaggtgggtg	atccgaggtg	cagctgctcg	agcagtctgg	agctgagctg	780
gcgaggcctg	gggcttcagt	gaagctgtcc	tgcaaggctt	ctggctacac	cttcacaaac	840
tatggtttaa	gctgggtgaa	gcagaggcct	ggacagggtc	ttgagtggat	tggagaggtt	900
tatcctagaa	ttggtaatgc	ttactacaat	gagaagttca	agggcaaggc	cacactgact	960
gcagacaaat	cctccagcac	agcgtccatg	gagctccgca	gcctgacctc	tgaggactct	1020
gcggtctatt	tctgtgcaag	acggggatcc	tacgatacta	actacgactg	gtacttcgat	1080
gtctggggcc	aagggaaccac	ggtcaccgtc	tcctcaggtg	gtggtgggtc	tggcggcggc	1140
ggctccgggtg	gtggtgggtc	tgagctcgtg	atgacccaga	ctccactctc	cctgcctgtc	1200
agtcttggag	atcaagcctc	catctcttgc	agatctagtc	agagccttgt	acacagtaat	1260
ggaaacacct	atttacattg	gtacctgcag	aagccaggcc	agtctccaaa	gctcctgata	1320
tacaaagttt	ccaaccgatt	ttctgggggtc	ccagacaggt	tcagtggcag	tggatcaggg	1380
acagatttca	cactcaagat	cagcagagtg	gaggctgagg	atctgggagt	ttatttctgc	1440
tctcaaagta	cacatgttcc	gtacacgttc	ggagggggga	ccaagcttga	gatcaaaa	1497

<210> 291

<211> 499

<212> PRT

<213> artificial sequence

<220>

<223> VL2/VH5x4-7 LHHL

<400> 291

Asp	Ile	Val	Leu	Thr	Gln	Ser	Pro	Ala	Thr	Leu	Ser	Leu	Ser	Pro	Gly
1				5					10					15	

Glu	Arg	Ala	Thr	Leu	Ser	Cys	Arg	Ala	Ser	Gln	Ser	Val	Ser	Tyr	Met
			20					25					30		

Asn	Trp	Tyr	Gln	Gln	Lys	Pro	Gly	Lys	Ala	Pro	Lys	Arg	Trp	Ile	Tyr
-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----

35 40 272 45

Asp Thr ser Lys val Ala ser Gly val Pro Ala Arg Phe ser Gly Ser
50 55 60

Gly ser Gly Thr Asp Tyr ser Leu Thr Ile Asn ser Leu Glu Ala Glu
65 70 75 80

Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp ser ser Asn Pro Leu Thr
85 90 95

Phe Gly Gly Gly Thr Lys val Glu Ile Lys Gly Glu Gly Thr ser Thr
100 105 110

Gly ser Gly Gly ser Gly Gly ser Gly Gly Ala Asp Asp val Gln Leu
115 120 125

val Gln ser Gly Ala Glu val Lys Lys Pro Gly Ala ser val Lys val
130 135 140

ser Cys Lys Ala ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp
145 150 155 160

val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn
165 170 175

Pro ser Arg Gly Tyr Thr Asn Tyr Ala Asp ser val Lys Gly Arg Phe
180 185 190

Thr Ile Thr Thr Asp Lys ser Thr ser Thr Ala Tyr Met Glu Leu ser
195 200 205

ser Leu Arg ser Glu Asp Thr Ala Thr Tyr Tyr Cys Ala Arg Tyr Tyr
210 215 220

Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr val Thr
225 230 235 240

val ser ser Gly Gly Gly Gly ser Glu val Gln Leu Leu Glu Gln ser
245 250 255

Gly Ala Glu Leu Ala Arg Pro Gly Ala ser val Lys Leu ser Cys Lys
260 265 270

Ala ser Gly Tyr Thr Phe Thr Asn Tyr Gly Leu ser Trp val Lys Gln
275 280 285

Arg Pro Gly Gln val Leu Glu Trp Ile Gly Glu val Tyr Pro Arg Ile
290 295 300

Gly Asn Ala Tyr Tyr Asn Glu Lys Phe Lys Gly Lys Ala Thr Leu Thr
305 310 315 320

Ala Asp Lys Ser Ser Ser Thr Ala Ser Met Glu Leu Arg Ser Leu Thr
 325 330 335

Ser Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg Arg Gly Ser Tyr Asp
 340 345 350

Thr Asn Tyr Asp Trp Tyr Phe Asp Val Trp Gly Gln Gly Thr Thr Val
 355 360 365

Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
 370 375 380

Gly Gly Ser Glu Leu Val Met Thr Gln Thr Pro Leu Ser Leu Pro Val
 385 390 395 400

Ser Leu Gly Asp Gln Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu
 405 410 415

Val His Ser Asn Gly Asn Thr Tyr Leu His Trp Tyr Leu Gln Lys Pro
 420 425 430

Gly Gln Ser Pro Lys Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser
 435 440 445

Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr
 450 455 460

Leu Lys Ile Ser Arg Val Glu Ala Glu Asp Leu Gly Val Tyr Phe Cys
 465 470 475 480

Ser Gln Ser Thr His Val Pro Tyr Thr Phe Gly Gly Gly Thr Lys Leu
 485 490 495

Glu Ile Lys

<210> 292

<211> 1497

<212> DNA

<213> artificial sequence

<220>

<223> VL2/VH5x4-7 LHLH

<400> 292

gacattgtac tgaccagtc tccagcaact ctgtctctgt ctccagggga gcgtgccacc 60

ctgagctgca gagccagtca aagtgttaagt tacatgaact ggtaccagca gaagccgggc 120

274

aaggcaccca aaagatggat ttatgacaca tccaaagtgg cttctggagt ccctgctcgc	180
ttcagtggca gtgggtcttg gaccgactac tctctcacia tcaacagctt ggaggctgaa	240
gatgctgccca cttattactg ccaacagtgg agtagtaacc cgctcacgtt cgggtggcggg	300
accaaggtgg agatcaaagg cgaaggtact agtactgggt ctggtggaag tggagggttca	360
gggtggagcag acgacgtcca actggtgcag tcaggggctg aagtgaaaaa acctggggcc	420
tcagtgaagg tgtcctgcaa ggcttctggc tacaccttta ctaggtacac gatgcactgg	480
gtaaggcagg cacctggaca gggctctggaa tggattggat acattaatcc tagccgtgg	540
tatactaatt acgcagacag cgtcaagggc cgcttcacia tcactacaga caaatccacc	600
agcacagcct acatggaact gagcagcctg cgttctgagg aactgcaac ctattactgt	660
gcaagatatt atgatgatca ttactgcctt gactactggg gccaaggcac cacggtcacc	720
gtctcctccg gaggtgggtg atccgagctc gtgatgacc agactccact ctccctgcct	780
gtcagtcttg gagatcaagc ctccatctct tgcagatcta gtcagagcct tgtacacagt	840
aatggaaaca cctatttaca ttggtacctg cagaagccag gccagtctcc aaagctcctg	900
atctacaaag tttccaaccg attttctggg gtcccagaca ggttcagtgg cagtggatca	960
gggacagatt tcacactcaa gatcagcaga gtggaggctg aggatctggg agttttatttc	1020
tgctctcaaa gtacacatgt tccgtacacg ttcggagggg ggaccaagct tgagatcaaa	1080
gggtggtggtg gttctggcgg cggcggctcc ggtggtggtg gttctgaggt gcagctgctc	1140
gagcagtctg gagctgagct ggcgaggcct ggggcttcag tgaagctgtc ctgcaaggct	1200
tctggctaca ccttcacaaa ctatgggttta agctgggtga agcagaggcc tggacaggctc	1260
cttgagtgga ttggagaggt ttatcctaga attggtaatg cttactacaa tgagaagttc	1320
aagggcaagg ccacactgac tgcagacaaa tcctccagca cagcgtccat ggagctccgc	1380
agcctgacct ctgaggactc tgcggtctat ttctgtgcaa gacggggatc ctacgatact	1440
aactacgact ggtacttcga tgtctggggc caagggacca cggtcaccgt ctctca	1497

<210> 293

<211> 499

<212> PRT

<213> artificial sequence

<220>

<223> VL2/VH5x4-7 LHLH

<400> 293

Asp	Ile	Val	Leu	Thr	Gln	Ser	Pro	Ala	Thr	Leu	Ser	Leu	Ser	Pro	Gly
1				5					10					15	

Glu	Arg	Ala	Thr	Leu	Ser	Cys	Arg	Ala	Ser	Gln	Ser	Val	Ser	Tyr	Met
			20					25					30		

Asn Trp Tyr₃₅ Gln Gln Lys Pro Gly₄₀ Lys Ala Pro Lys Arg₄₅ Trp Ile Tyr
 Asp Thr₅₀ Ser Lys Val Ala Ser₅₅ Gly Val Pro Ala Arg₆₀ Phe Ser Gly Ser
 Gly₆₅ Ser Gly Thr Asp Tyr₇₀ Ser Leu Thr Ile Asn₇₅ Ser Leu Glu Ala Glu₈₀
 Asp Ala Ala Thr Tyr₈₅ Tyr Cys Gln Gln Trp₉₀ Ser Ser Asn Pro Leu Thr
 Phe Gly Gly Gly₁₀₀ Thr Lys Val Glu Ile₁₀₅ Lys Gly Glu Gly Thr₁₁₀ Ser Thr
 Gly Ser Gly₁₁₅ Gly Ser Gly Gly Ser₁₂₀ Gly Gly Ala Asp Asp₁₂₅ Val Gln Leu
 Val Gln₁₃₀ Ser Gly Ala Glu Val₁₃₅ Lys Lys Pro Gly Ala₁₄₀ Ser Val Lys Val
 Ser₁₄₅ Cys Lys Ala Ser Gly₁₅₀ Tyr Thr Phe Thr Arg₁₅₅ Tyr Thr Met His Trp₁₆₀
 Val Arg Gln Ala Pro₁₆₅ Gly Gln Gly Leu Glu₁₇₀ Trp Ile Gly Tyr Ile Asn₁₇₅
 Pro Ser Arg Gly₁₈₀ Tyr Thr Asn Tyr Ala₁₈₅ Asp Ser Val Lys Gly₁₉₀ Arg Phe
 Thr Ile Thr₁₉₅ Thr Asp Lys Ser Thr₂₀₀ Ser Thr Ala Tyr Met₂₀₅ Glu Leu Ser
 Ser₂₁₀ Leu Arg Ser Glu Asp Thr₂₁₅ Ala Thr Tyr Tyr Cys₂₂₀ Ala Arg Tyr Tyr
 Asp₂₂₅ Asp His Tyr Cys Leu₂₃₀ Asp Tyr Trp Gly Gln₂₃₅ Gly Thr Thr Val Thr₂₄₀
 Val Ser Ser Gly Gly₂₄₅ Gly Gly Ser Glu Leu Val Met Thr Gln Thr Pro₂₅₅
 Leu Ser Leu Pro₂₆₀ Val Ser Leu Gly Asp₂₆₅ Gln Ala Ser Ile Ser Cys Arg
 Ser Ser Gln₂₇₅ Ser Leu Val His Ser₂₈₀ Asn Gly Asn Thr Tyr₂₈₅ Leu His Trp
 Tyr Leu₂₉₀ Gln Lys Pro Gly Gln₂₉₅ Ser Pro Lys Leu Leu₃₀₀ Ile Tyr Lys Val

276

Ser Asn Arg Phe Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser
305 310 315 320

Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu Asp Leu
325 330 335

Gly Val Tyr Phe Cys Ser Gln Ser Thr His Val Pro Tyr Thr Phe Gly
340 345 350

Gly Gly Thr Lys Leu Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly Gly
355 360 365

Gly Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Leu Glu Gln Ser Gly
370 375 380

Ala Glu Leu Ala Arg Pro Gly Ala Ser Val Lys Leu Ser Cys Lys Ala
385 390 395 400

Ser Gly Tyr Thr Phe Thr Asn Tyr Gly Leu Ser Trp Val Lys Gln Arg
405 410 415

Pro Gly Gln Val Leu Glu Trp Ile Gly Glu Val Tyr Pro Arg Ile Gly
420 425 430

Asn Ala Tyr Tyr Asn Glu Lys Phe Lys Gly Lys Ala Thr Leu Thr Ala
435 440 445

Asp Lys Ser Ser Ser Thr Ala Ser Met Glu Leu Arg Ser Leu Thr Ser
450 455 460

Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg Arg Gly Ser Tyr Asp Thr
465 470 475 480

Asn Tyr Asp Trp Tyr Phe Asp Val Trp Gly Gln Gly Thr Thr Val Thr
485 490 495

Val Ser Ser

<210> 294

<211> 1497

<212> DNA

<213> artificial sequence

<220>

<223> VL3VH5x4-7 LHHL

<400> 294

gacattgtac tgaccagtc tccagcaact ctgtctctgt ctccagggga gcgtgccacc

```

ctgacctgca gagccagttc aagtgttaagt tacatgaact ggtaccagca gaagccgggc 120
aaggcaccca aaagatggat ttatgacaca tccaaagtgg cttctggagt ccctgctcgc 180
ttcagtggca gtgggtcttg gaccgactac tctctcacia tcaacagctt ggaggctgaa 240
gatgctgcca cttattactg ccaacagtgg agtagtaacc cgctcacgtt cgggtggcggg 300
accaaggtgg agatcaaagg cgaagggtact agtactgggt ctggtggaag tggaggttca 360
ggtggagcag acgacgtcca actggtgcag tcaggggctg aagtgaaaaa acctggggcc 420
tcagtgaagg tgtcctgcaa ggcttctggc tacaccttta ctaggtacac gatgcactgg 480
gtaaggcagg cacctggaca ggttctggaa tggattggat acattaatcc tagccgtggt 540
tatactaatt acgcagacag cgtcaagggc cgcttcacia tcactacaga caaatccacc 600
agcacagcct acatggaact gagcagcctg cgcttctgagg aactgcaac ctattactgt 660
gcaagatatt atgatgatca ttactgcctt gactactggg gccaaggcac cacggtcacc 720
gtctcctccg gaggtgggtg atccgaggtg cagctgctcg agcagtctgg agctgagctg 780
gcgaggcctg gggcttcagt gaagctgtcc tgcaaggctt ctggctacac cttcaciaaac 840
tatggtttaa gctgggtgaa gcagaggcct ggacaggctc ttgagtggat tggagagggt 900
tatacctaga ttggtaatgc ttactacaat gagaagttca agggcaaggc cacactgact 960
gcagacaaat cctccagcac agcgtccatg gagctccgca gcctgacctc tgaggactct 1020
gcggtctatt tctgtgcaag acggggatcc tacgatacta actacgactg gtacttcgat 1080
gtctggggcc aagggaccac ggtcaccgtc tcctcaggtg gtggtgggtc tggcggcggc 1140
ggctccggtg gtggtgggtc tgagctcgtg atgaccaga ctccactctc cctgcctgtc 1200
agtcttggag atcaagcctc catctcttgc agatctagtc agagccttgt acacagtaat 1260
ggaaacacct atttacattg gtacctgcag aagccaggcc agtctccaaa gctcctgatc 1320
taciaaagttt ccaaccgatt ttctggggtc ccagacaggt tcagtggcag tggatcaggg 1380
acagatttca cactcaagat cagcagagtg gaggctgagg atctgggagt ttatttctgc 1440
tctcaaagta cacatgttcc gtacacgttc ggagggggga ccaagcttga gatcaaa 1497

```

<210> 295

<211> 499

<212> PRT

<213> artificial sequence

<220>

<223> VL3/VH5x4-7 LHHL

<400> 295

Asp Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
1 5 10 15

Glu Arg Ala Thr Leu Thr Cys Arg Ala Ser Ser Ser Val Ser Tyr Met
20 25 30

Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr
35 40 45

Asp Thr Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
50 55 60

Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu
65 70 75 80

Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr
85 90 95

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Gly Glu Gly Thr Ser Thr
100 105 110

Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Val Gln Leu
115 120 125

Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val
130 135 140

Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp
145 150 155 160

Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn
165 170 175

Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val Lys Gly Arg Phe
180 185 190

Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser
195 200 205

Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys Ala Arg Tyr Tyr
210 215 220

Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr
225 230 235 240

Val Ser Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Leu Glu Gln Ser
245 250 255

Gly Ala Glu Leu Ala Arg Pro Gly Ala Ser Val Lys Leu Ser Cys Lys
260 265 270

Ala Ser Gly Tyr Thr Phe Thr Asn Tyr Gly Leu Ser Trp Val Lys Gln
275 280 285

Arg Pro Gly Gln Val Leu Glu Trp Ile Gly Glu Val Tyr Pro Arg Ile
290 295 300 279

Gly Asn Ala Tyr Tyr Asn Glu Lys Phe Lys Gly Lys Ala Thr Leu Thr
305 310 315 320

Ala Asp Lys Ser Ser Ser Thr Ala Ser Met Glu Leu Arg Ser Leu Thr
325 330 335

Ser Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg Arg Gly Ser Tyr Asp
340 345 350

Thr Asn Tyr Asp Trp Tyr Phe Asp Val Trp Gly Gln Gly Thr Thr Val
355 360 365

Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
370 375 380

Gly Gly Ser Glu Leu Val Met Thr Gln Thr Pro Leu Ser Leu Pro Val
385 390 395 400

Ser Leu Gly Asp Gln Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu
405 410 415

Val His Ser Asn Gly Asn Thr Tyr Leu His Trp Tyr Leu Gln Lys Pro
420 425 430

Gly Gln Ser Pro Lys Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser
435 440 445

Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr
450 455 460

Leu Lys Ile Ser Arg Val Glu Ala Glu Asp Leu Gly Val Tyr Phe Cys
465 470 475 480

Ser Gln Ser Thr His Val Pro Tyr Thr Phe Gly Gly Gly Thr Lys Leu
485 490 495

Glu Ile Lys

<210> 296

<211> 1503

<212> DNA

<213> artificial sequence

<220>

<223> VH5VL3x4-7 HLHL

<400> 296
 gacgtccaac tgggtgcagtc aggggctgaa gtgaaaaaac ctggggcctc agtgaagggtg 60
 tcctgcaagg cttctggcta cacctttact aggtacacga tgcactgggt aaggcaggca 120
 cctggacagg gtctggaatg gattggatac attaatccta gccgtgggta tactaattac 180
 gcagacagcg tcaagggccg cttcacaatc actacagaca aatccaccag cacagcctac 240
 atggaactga gcagcctgcg ttctgaggac actgcaacct attactgtgc aagatattat 300
 gatgatcatt actgccttga ctactggggc caaggcacca cggtcaccgt ctctcagggc 360
 gaagggtacta gtactgggtc tgggtggaagt ggagggttcag gtggagcaga cgacattgta 420
 ctgacccagt ctccagcaac tctgtctctg tctccagggg agcgtgccac cctgacctgc 480
 agagccagtt caagtgtaag ttacatgaac tgggtaccagc agaagccggg caaggcaccc 540
 aaaagatgga tttatgacac atccaaagtg gcttctggag tccctgctcg cttcagtggc 600
 agtgggtctg ggaccgacta ctctctcaca atcaacagct tggaggctga agatgctgcc 660
 acttattact gccaacagtg gagtagtaac ccgctcacgt tcggtggcgg gaccaagggtg 720
 gagatcaaatt ccggagggtg tggatccgag gtgcagctgc tcgagcagtc tggagctgag 780
 ctggcgaggc ctggggcttc agtgaagctg tcctgcaagg cttctggcta caccttcaca 840
 aactatgggt taagctgggt gaagcagagg cctggacagg tccttgagtg gattggagag 900
 gtttatccta gaattggtaa tgcttactac aatgagaagt tcaagggcaa ggccacactg 960
 actgcagaca aatcctccag cacagcgtcc atggagctcc gcagcctgac ctctgaggac 1020
 tctgcggtct atttctgtgc aagacgggga tcctacgata ctaactacga ctggtacttc 1080
 gatgtctggg gccaaaggac cacggtcacc gtctcctcag gtggtgggtg ttctggcggc 1140
 ggcggctccg gtggtgggtg ttctgagctc gtgatgacct agactccact ctccctgcct 1200
 gtcagtcttg gagatcaagc ctccatctct tgcagatcta gtcagagcct tgtacacagt 1260
 aatggaaaca cctatttaca ttggtacctg cagaagccag gccagtctcc aaagctcctg 1320
 atctacaaag tttccaaccg attttctggg gtcccagaca ggttcagtgg cagtggatca 1380
 gggacagatt tcacactcaa gatcagcaga gtggaggctg aggatctggg agtttatttc 1440
 tgctctcaaa gtacacatgt tccgtacacg ttcggagggg ggaccaagct tgagatcaaa 1500
 cat 1503

<210> 297

<211> 500

<212> PRT

<213> artificial sequence

<220>

<223> VH5VL3x4-7 HLHL

<400> 297

Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
 1 5 10 15
 Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr
 20 25 30
 Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
 35 40 45
 Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val
 50 55 60
 Lys Gly Arg Phe Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr
 65 70 75 80
 Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys
 85 90 95
 Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
 100 105 110
 Thr Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly
 115 120 125
 Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Val Leu Thr Gln Ser
 130 135 140
 Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Thr Cys
 145 150 155 160
 Arg Ala Ser Ser Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro
 165 170 175
 Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser
 180 185 190
 Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser
 195 200 205
 Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys
 210 215 220
 Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
 225 230 235 240
 Glu Ile Lys Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Leu Glu Gln
 245 250 255
 Ser Gly Ala Glu Leu Ala Arg Pro Gly Ala Ser Val Lys Leu Ser Cys
 260 265 270

Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr Gly Leu Ser Trp Val Lys
 275 280 285

Gln Arg Pro Gly Gln Val Leu Glu Trp Ile Gly Glu Val Tyr Pro Arg
 290 295 300

Ile Gly Asn Ala Tyr Tyr Asn Glu Lys Phe Lys Gly Lys Ala Thr Leu
 305 310 315 320

Thr Ala Asp Lys Ser Ser Ser Thr Ala Ser Met Glu Leu Arg Ser Leu
 325 330 335

Thr Ser Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg Arg Gly Ser Tyr
 340 345 350

Asp Thr Asn Tyr Asp Trp Tyr Phe Asp Val Trp Gly Gln Gly Thr Thr
 355 360 365

Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
 370 375 380

Gly Gly Gly Ser Glu Leu Val Met Thr Gln Thr Pro Leu Ser Leu Pro
 385 390 395 400

Val Ser Leu Gly Asp Gln Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser
 405 410 415

Leu Val His Ser Asn Gly Asn Thr Tyr Leu His Trp Tyr Leu Gln Lys
 420 425 430

Pro Gly Gln Ser Pro Lys Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe
 435 440 445

Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe
 450 455 460

Thr Leu Lys Ile Ser Arg Val Glu Ala Glu Asp Leu Gly Val Tyr Phe
 465 470 475 480

Cys Ser Gln Ser Thr His Val Pro Tyr Thr Phe Gly Gly Gly Thr Lys
 485 490 495

Leu Glu Ile Lys
 500

<210> 298

<211> 1497

<212> DNA

<213> artificial sequence

<220>

<223> VL3VH5x4-7 LHLH

<400> 298

gacattgtac	tgacccagtc	tccagcaact	ctgtctctgt	ctccagggga	gcgtgccacc	60
ctgacctgca	gagccagttc	aagtgttaagt	tacatgaact	ggtaccagca	gaagccgggc	120
aaggcaccca	aaagatggat	ttatgacaca	tccaaagtgg	cttctggagt	ccctgctcgc	180
ttcagtggca	gtgggtctgg	gaccgactac	tctctcacia	tcaacagctt	ggaggctgaa	240
gatgctgcca	cttattactg	ccaacagtgg	agtagtaacc	cgctcacgtt	cggtggcggg	300
accaaggtgg	agatcaaagg	cgaaggtact	agtactgggt	ctggtggaag	tggagggttca	360
ggtggagcag	acgacgtcca	actggtgcag	tcaggggctg	aagtgaaaaa	acctggggcc	420
tcagtgaagg	tgtcctgcaa	ggcttctggc	tacaccttta	ctaggtagac	gatgcactgg	480
gtaaggcagg	cacctggaca	gggtctggaa	tggattggat	acattaatcc	tagccgtggg	540
tatactaatt	acgcagacag	cgtcaagggc	cgcttcacia	tcactacaga	caaattccacc	600
agcacagcct	acatggaact	gagcagcctg	cgcttctgagg	acactgcaac	ctattactgt	660
gcaagatatt	atgatgatca	ttactgcctt	gactactggg	gccaaaggcac	cacggtcacc	720
gtctcctccg	gaggtgggtg	atccgagctc	gtgatgacct	agactccact	ctccctgcct	780
gtcagtcttg	gagatcaagc	ctccatctct	tgcagatcta	gtcagagcct	tgtacacagt	840
aatggaaaca	cctattttaca	ttggtacctg	cagaagccag	gccagtctcc	aaagctcctg	900
atctacaaag	tttccaaccg	attttctggg	gtcccagaca	ggttcagtgg	cagtggatca	960
gggacagatt	tcacactcaa	gatcagcaga	gtggaggctg	aggatctggg	agttttatttc	1020
tgctctcaaa	gtacacatgt	tccgtacacg	ttcggagggg	ggaccaagct	tgagatcaaa	1080
ggtggtggtg	gttctggcgg	cggcggctcc	ggtggtggtg	gttctgaggt	gcagctgctc	1140
gagcagtctg	gagctgagct	ggcgaggcct	ggggcttcag	tgaagctgtc	ctgcaaggct	1200
tctggctaca	ccttcacaaa	ctatgggttta	agctgggtga	agcagaggcc	tggacaggctc	1260
cttgagtgga	ttggagaggt	ttatcctaga	attggtaatg	cttactacaa	tgagaagttc	1320
aagggcaagg	ccacactgac	tgcagacaaa	tcctccagca	cagcgtccat	ggagctccgc	1380
agcctgacct	ctgaggactc	tgcggtctat	ttctgtgcaa	gacggggatc	ctacgatact	1440
aactacgact	ggtacttcga	tgtctggggc	caagggacca	cggtcaccgt	ctcctca	1497

<210> 299

<211> 499

<212> PRT

<213> artificial sequence

<220>

<223> VL3/VH5x4-7 LHLH

<400> 299

Asp Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
 1 5 10 15

Glu Arg Ala Thr Leu Thr Cys Arg Ala Ser Ser Ser Val Ser Tyr Met
 20 25 30

Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr
 35 40 45

Asp Thr Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
 50 55 60

Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu
 65 70 75 80

Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr
 85 90 95

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Gly Glu Gly Thr Ser Thr
 100 105 110

Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Val Gln Leu
 115 120 125

Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val
 130 135 140

Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp
 145 150 155 160

Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn
 165 170 175

Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val Lys Gly Arg Phe
 180 185 190

Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser
 195 200 205

Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys Ala Arg Tyr Tyr
 210 215 220

Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr
 225 230 235 240

Val Ser Ser Gly Gly Gly Gly Ser Glu Leu Val Met Thr Gln Thr Pro
 245 250 255

Leu Ser Leu Pro Val Ser Leu Gly Asp Gln²⁸⁵ Ala Ser Ile Ser Cys Arg
 260 265 270
 Ser Ser Gln Ser Leu Val His Ser Asn Gly Asn Thr Tyr Leu His Trp
 275 280 285
 Tyr Leu Gln Lys Pro Gly Gln Ser Pro Lys Leu Leu Ile Tyr Lys Val
 290 295 300
 Ser Asn Arg Phe Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser
 305 310 315 320
 Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu Asp Leu
 325 330 335
 Gly Val Tyr Phe Cys Ser Gln Ser Thr His Val Pro Tyr Thr Phe Gly
 340 345 350
 Gly Gly Thr Lys Leu Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly Gly
 355 360 365
 Gly Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Leu Glu Gln Ser Gly
 370 375 380
 Ala Glu Leu Ala Arg Pro Gly Ala Ser Val Lys Leu Ser Cys Lys Ala
 385 390 395 400
 Ser Gly Tyr Thr Phe Thr Asn Tyr Gly Leu Ser Trp Val Lys Gln Arg
 405 410 415
 Pro Gly Gln Val Leu Glu Trp Ile Gly Glu Val Tyr Pro Arg Ile Gly
 420 425 430
 Asn Ala Tyr Tyr Asn Glu Lys Phe Lys Gly Lys Ala Thr Leu Thr Ala
 435 440 445
 Asp Lys Ser Ser Ser Thr Ala Ser Met Glu Leu Arg Ser Leu Thr Ser
 450 455 460
 Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg Arg Gly Ser Tyr Asp Thr
 465 470 475 480
 Asn Tyr Asp Trp Tyr Phe Asp Val Trp Gly Gln Gly Thr Thr Val Thr
 485 490 495
 Val Ser Ser

<210> 300

<211> 1500

<212> DNA

<213> artificial sequence

<220>

<223> VH5VL3x4-7 HLLH

<400> 300
gacgtccâac tgggtgcagtc aggggctgaa gtgaaaaaac ctggggcctc agtgaagggtg 60
tcctgcaagg cttctggcta cacctttact aggtacacga tgcactgggt aaggcaggca 120
cctggacagg gtctggaatg gattggatac attaatccta gccgtggtta tactaattac 180
gcagacagcg tcaagggccg cttcacaatc actacagaca aatccaccag cacagcctac 240
atggaactga gcagcctgcg ttctgaggac actgcaacct attactgtgc aagatattat 300
gatgatcatt actgccttga ctactggggc caaggcacca cggtcaccgt ctcctcaggc 360
gaaggtaacta gtactgggttc tgggtggaagt ggagggttcag gtggagcaga cgacattgta 420
ctgacccagt ctccagcaac tctgtctctg tctccagggg agcgtgccac cctgacctgc 480
agagccagtt caagtgtaag ttacatgaac tgggtaccagc agaagccggg caaggcaccc 540
aaaagatgga tttatgacac atccaaagtg gcttctggag tccctgctcg cttcagtggc 600
agtgggtctg ggaccgacta ctctctcaca atcaacagct tggaggctga agatgctgcc 660
acttattact gccaacagtg gagtagtaac ccgctcacgt tcggtggcgg gaccaagggtg 720
gagatcaaâat ccggagggtgg tggatccgag ctcgtgatga cccagactcc actctccctg 780
cctgtcagtc ttggagatca agcctccatc tcttgcagat ctagtcagag ctttgtacac 840
agtaatggaa acacctatââ acattgggtac ctgcagaagc caggccagtc tccaaagctc 900
ctgatctaca aagtttccaa ccgattttct ggggtcccag acagggttcag tggcagtgga 960
tcagggacag atttcacact caagatcagc agagtggagg ctgaggatct gggagtttat 1020
ttctgctctc aaagtacaca tgttccgtac acgttcggag gggggaccaa gcttgagatc 1080
aaagggtggtg gtggttcttg cggcggcggc tccggtggtg gtggttctga ggtgcagctg 1140
ctcgagcagt ctggagctga gctggcgagg cctggggctt cagtgaagct gtcctgcaag 1200
gcttctggct acaccttcac aaactatggt ttaagctggg tgaagcagag gcctggacag 1260
gtccttgagt ggattggaga ggtttatcct agaattggta atgcttacta caatgagaag 1320
ttcaagggca aggccacact gactgcagac aaatcctcca gcacagcgtc catggagctc 1380
cgcagcctga cctctgagga ctctgcggtc tâtâââctgtg caagacgggg atcctacgat 1440
actaactacg actggtactt cgatgtctgg ggccaaggga ccacggtcac cgtctcctca 1500

<210> 301

<211> 500

<212> PRT

<213> artificial sequence

<220>

<223> VH5VL3x4-7 HLLH

<400> 301

Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr
20 25 30

Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys
85 90 95

Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly
115 120 125

Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Val Leu Thr Gln Ser
130 135 140

Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Thr Cys
145 150 155 160

Arg Ala Ser Ser Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro
165 170 175

Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser
180 185 190

Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser
195 200 205

Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys
210 215 220

Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
225 230 235 240

Glu Ile Lys Ser Gly Gly Gly Gly Ser Glu Leu Val Met Thr Gln Thr

245 288 255
 250
 Pro Leu Ser Leu Pro Val Ser Leu Gly Asp Gln Ala Ser Ile Ser Cys
 260 265 270
 Arg Ser Ser Gln Ser Leu Val His Ser Asn Gly Asn Thr Tyr Leu His
 275 280 285
 Trp Tyr Leu Gln Lys Pro Gly Gln Ser Pro Lys Leu Leu Ile Tyr Lys
 290 295 300
 Val Ser Asn Arg Phe Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly
 305 310 315 320
 Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu Asp
 325 330 335
 Leu Gly Val Tyr Phe Cys Ser Gln Ser Thr His Val Pro Tyr Thr Phe
 340 345 350
 Gly Gly Gly Thr Lys Leu Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly
 355 360 365
 Gly Gly Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Leu Glu Gln Ser
 370 375 380
 Gly Ala Glu Leu Ala Arg Pro Gly Ala Ser Val Lys Leu Ser Cys Lys
 385 390 395 400
 Ala Ser Gly Tyr Thr Phe Thr Asn Tyr Gly Leu Ser Trp Val Lys Gln
 405 410 415
 Arg Pro Gly Gln Val Leu Glu Trp Ile Gly Glu Val Tyr Pro Arg Ile
 420 425 430
 Gly Asn Ala Tyr Tyr Asn Glu Lys Phe Lys Gly Lys Ala Thr Leu Thr
 435 440 445
 Ala Asp Lys Ser Ser Ser Thr Ala Ser Met Glu Leu Arg Ser Leu Thr
 450 455 460

 Ser Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg Arg Gly Ser Tyr Asp
 465 470 475 480
 Thr Asn Tyr Asp Trp Tyr Phe Asp Val Trp Gly Gln Gly Thr Thr Val
 485 490 495
 Thr Val Ser Ser
 500

<211> 1497

<212> DNA

<213> artificial sequence

<220>

<223> VL1VH7x4-7 LHHL

<400> 302

gacattcaga	tgacccagtc	tccatctagc	ctgtctgcat	ctgtcgggga	ccgtgtcacc	60
atcacctgca	gagccagtc	aagtgtatgt	tacatgaact	ggtaccagca	gaagccgggc	120
aaggcacc	aaagatggat	ttatgacaca	tccaaagtgg	cttctggagt	ccctgctcgc	180
ttcagtggca	gtgggtctgg	gaccgactac	tctctcaca	tcaacagctt	ggaggctgaa	240
gatgctgcca	cttattactg	ccaacagtgg	agtagtaacc	cgctcacgtt	cggtggcggg	300
accaaggtgg	agatcaaagg	cgaagggtact	agtactgggt	ctgggtggaag	tggagggttca	360
ggtggagcag	acgacgtcca	actgggtgcag	tcaggggctg	aagtgaaaaa	acctggggcc	420
tcagtgaagg	tgtcctgcaa	ggcttctggc	tacaccttta	ctagggtacac	gatgcactgg	480
gtaaggcagg	cacctggaca	gggtctggaa	tggattggat	acattaatcc	tagccgtgggt	540
tatactaatt	acaatcagaa	gttcaaggac	cgcgtcaca	tcactacaga	caaattccacc	600
agcacagcct	acatggaact	gagcagcctg	cggtctgagg	acactgcagt	ctattactgt	660
gcaagatatt	atgatgatca	ttactgcctt	gactactggg	gccaaggcac	cacggtcacc	720
gtctcctccg	gaggtgggtg	atccgaggtg	cagctgctcg	agcagtctgg	agctgagctg	780
gcgaggcctg	gggcttcagt	gaagctgtcc	tgcaaggctt	ctgggtacac	cttcacaaac	840
tatgggttta	gctgggtgaa	gcagaggcct	ggacagggtc	ttgagtggat	tggagagggtt	900
tatcctagaa	ttggtaatgc	ttactacaat	gagaagttca	agggcaaggc	cacactgact	960
gcagacaaat	cctccagcac	agcgtccatg	gagctccgca	gcctgacctc	tgaggactct	1020
gcggtctatt	tctgtgcaag	acgggggatcc	tacgatacta	actacgactg	gtacttcgat	1080
gtctggggcc	aagggaccac	ggtcaccgtc	tcctcaggtg	gtgggtgggtc	tggcggcggc	1140
ggctccgggtg	gtgggtgggtc	tgagctcgtg	atgaccacga	ctccactctc	cctgcctgtc	1200
agtcttggag	atcaagcctc	catctcttgc	agatctagtc	agagccttgt	acacagtaat	1260
ggaaacacct	atttacattg	gtacctgcag	aagccaggcc	agtctccaaa	gctcctgatc	1320
tacaaagttt	ccaaccgatt	ttctgggggtc	ccagacaggt	tcagtggcag	tggatcaggg	1380
acagatttca	cactcaagat	cagcagagtg	gaggctgagg	atctgggagt	ttatttctgc	1440
tctcaaagta	cacatgttcc	gtacacgttc	ggaggggggga	ccaagcttga	gatcaaaa	1497

<210> 303

<211> 499

<212> PRT

<213> artificial sequence

<220>

<223> VL1VH7x4-7 LHHL

<400> 303

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Ser Tyr Met
20 25 30

Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr
35 40 45

Asp Thr Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
50 55 60

Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu
65 70 75 80

Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr
85 90 95

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Gly Glu Gly Thr Ser Thr
100 105 110

Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Val Gln Leu
115 120 125

Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val
130 135 140

Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp
145 150 155 160

Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn
165 170 175

Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe Lys Asp Arg Val
180 185 190

Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser
195 200 205

Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Tyr Tyr
210 215 220

Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr
225 230 235 240

val Ser Ser Gly Gly Gly Gly Ser Glu val Gln Leu Leu Glu Gln Ser
 245 250 255
 Gly Ala Glu Leu Ala Arg Pro Gly Ala Ser val Lys Leu Ser Cys Lys
 260 265 270
 Ala Ser Gly Tyr Thr Phe Thr Asn Tyr Gly Leu Ser Trp Val Lys Gln
 275 280 285
 Arg Pro Gly Gln Val Leu Glu Trp Ile Gly Glu val Tyr Pro Arg Ile
 290 295 300
 Gly Asn Ala Tyr Tyr Asn Glu Lys Phe Lys Gly Lys Ala Thr Leu Thr
 305 310 315 320
 Ala Asp Lys Ser Ser Ser Thr Ala Ser Met Glu Leu Arg Ser Leu Thr
 325 330 335
 Ser Glu Asp Ser Ala val Tyr Phe Cys Ala Arg Arg Gly Ser Tyr Asp
 340 345 350
 Thr Asn Tyr Asp Trp Tyr Phe Asp val Trp Gly Gln Gly Thr Thr val
 355 360 365
 Thr val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
 370 375 380
 Gly Gly Ser Glu Leu val Met Thr Gln Thr Pro Leu Ser Leu Pro val
 385 390 395 400
 Ser Leu Gly Asp Gln Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu
 405 410 415
 val His Ser Asn Gly Asn Thr Tyr Leu His Trp Tyr Leu Gln Lys Pro
 420 425 430
 Gly Gln Ser Pro Lys Leu Leu Ile Tyr Lys val Ser Asn Arg Phe Ser
 435 440 445
 Gly val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr
 450 455 460
 Leu Lys Ile Ser Arg val Glu Ala Glu Asp Leu Gly val Tyr Phe Cys
 465 470 475 480
 Ser Gln Ser Thr His val Pro Tyr Thr Phe Gly Gly Gly Thr Lys Leu
 485 490 495
 Glu Ile Lys

<210> 304

<211> 1500

<212> DNA

<213> artificial sequence

<220>

<223> VH7-VL1x4-7 HLHL

<400> 304

gacgtccaac	tggtgcagtc	aggggctgaa	gtgaaaaaac	ctggggcctc	agtgaagggtg	60
tcctgcaagg	cttctggcta	cacctttact	aggtacacga	tgcactgggt	aaggcaggca	120
cctggacagg	gtctggaatg	gattggatac	attaatccta	gccgtggtta	tactaattac	180
aatcagaagt	tcaaggaccg	cgtcacaatc	actacagaca	aatccaccag	cacagcctac	240
atggaactga	gcagcctgcg	ttctgaggac	actgcagtct	attactgtgc	aagatattat	300
gatgatcatt	actgccttga	ctactggggc	caaggcacca	cggtcaccgt	ctcctcaggc	360
gaaggtaacta	gtactgggttc	tggtggaagt	ggagggttcag	gtggagcaga	cgacattcag	420
atgaccagtc	ctccatctag	cctgtctgca	tctgtcgggg	accgtgtcac	catcacctgc	480
agagccagtc	aaagtgtgtaag	ttacatgaac	tggtaccagc	agaagccggg	caaggcaccc	540
aaaagatgga	tttatgacac	atccaaagtg	gcttctggag	tccctgctcg	cttcagtggc	600
agtgggtctg	ggaccgacta	ctctctcaca	atcaacagct	tggaggctga	agatgctgcc	660
acttattact	gccaacagtg	gagtagtaac	ccgctcacgt	tcggtggcgg	gaccaagggtg	720
gagatcaaat	ccggagggtgg	tggatccgag	gtgcagctgc	tcgagcagtc	tggagctgag	780
ctggcgaggc	ctggggcttc	agtgaagctg	tcctgcaagg	cttctggcta	caccttcaca	840
aactatggtt	taagctgggt	gaagcagagg	cctggacagg	tccttgagtg	gattggagag	900
gtttatccta	gaattggtaa	tgcttactac	aatgagaagt	tcaagggcaa	ggccacactg	960
actgcagaca	aatcctccag	cacagcgtcc	atggagctcc	gcagcctgac	ctctgaggac	1020
tctgcggtct	atcttctgtgc	aagacgggga	tcctacgata	ctaactacga	ctggtacttc	1080
gatgtctggg	gccaagggac	cacggtcacc	gtctcctcag	gtggtggtgg	ttctggcggc	1140
ggcggctccg	gtggtggtgg	ttctgagctc	gtgatgaccc	agactccact	ctccctgcct	1200
gtcagtcttg	gagatcaagc	ctccatctct	tgcagatcta	gtcagagcct	tgtacacagt	1260
aatggaaaca	cctattttaca	ttggtacctg	cagaagccag	gccagtctcc	aaagctcctg	1320
atctacaaag	tttccaaccg	atcttctggg	gtcccagaca	ggttcagtgg	cagtggatca	1380
gggacagatt	tcacactcaa	gatcagcaga	gtggaggctg	aggatctggg	agttttatttc	1440
tgctctcaaa	gtacacatgt	tccgtacacg	ttcggagggg	ggaccaagct	tgagatcaaa	1500

<210> 305

<211> 500

<212> PRT

<213> artificial sequence

<220>

<223> VH7-VL1x4-7 HLHL

<400> 305

Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
 1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr
 20 25 30

Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
 35 40 45

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe
 50 55 60

Lys Asp Arg Val Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr
 65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
 85 90 95

Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
 100 105 110

Thr Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly
 115 120 125

Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Gln Met Thr Gln Ser
 130 135 140

Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys
 145 150 155 160

Arg Ala Ser Gln Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro
 165 170 175

Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser
 180 185 190

Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser
 195 200 205

Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys
 210 215 220

Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
225 230 235 240

Glu Ile Lys Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Leu Glu Gln
245 250 255

Ser Gly Ala Glu Leu Ala Arg Pro Gly Ala Ser Val Lys Leu Ser Cys
260 265 270

Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr Gly Leu Ser Trp Val Lys
275 280 285

Gln Arg Pro Gly Gln Val Leu Glu Trp Ile Gly Glu Val Tyr Pro Arg
290 295 300

Ile Gly Asn Ala Tyr Tyr Asn Glu Lys Phe Lys Gly Lys Ala Thr Leu
305 310 315 320

Thr Ala Asp Lys Ser Ser Ser Thr Ala Ser Met Glu Leu Arg Ser Leu
325 330 335

Thr Ser Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg Arg Gly Ser Tyr
340 345 350

Asp Thr Asn Tyr Asp Trp Tyr Phe Asp Val Trp Gly Gln Gly Thr Thr
355 360 365

Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
370 375 380

Gly Gly Gly Ser Glu Leu Val Met Thr Gln Thr Pro Leu Ser Leu Pro
385 390 395 400

Val Ser Leu Gly Asp Gln Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser
405 410 415

Leu Val His Ser Asn Gly Asn Thr Tyr Leu His Trp Tyr Leu Gln Lys
420 425 430

~~Pro Gly Gln Ser Pro Lys Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe~~
435 440 445

Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe
450 455 460

Thr Leu Lys Ile Ser Arg Val Glu Ala Glu Asp Leu Gly Val Tyr Phe
465 470 475 480

Cys Ser Gln Ser Thr His Val Pro Tyr Thr Phe Gly Gly Gly Thr Lys
485 490 495

Leu Glu Ile Lys
500

<210> 306

<211> 1497

<212> DNA

<213> artificial sequence

<220>

<223> VL1-VH7x4-7 LHLH

<400> 306

gacattcaga	tgacccagtc	tccatctagc	ctgtctgcat	ctgtcgggga	ccgtgtcacc	60
atcacctgca	gagccagtca	aagtgtaagt	tacatgaact	ggtaccagca	gaagccgggc	120
aaggcaccca	aaagatggat	ttatgacaca	tccaaagtgg	cttctggagt	ccctgctcgc	180
ttcagtggca	gtgggtctgg	gaccgactac	tctctcaca	tcaacagctt	ggaggctgaa	240
gatgctgcca	cttattactg	ccaacagtgg	agtagtaacc	cgctcacgtt	cggtggcggg	300
accaaggtgg	agatcaaagg	cgaagggtact	agtactgggt	ctgggtggaag	tggagggttca	360
ggtggagcag	acgacgtcca	actgggtgcag	tcaggggctg	aagtgaaaaa	acctggggcc	420
tcagtgaagg	tgtcctgcaa	ggcttctggc	tacaccttta	ctaggtacac	gatgcactgg	480
gtaaggcagg	cacctggaca	gggtctggaa	tggattggat	acattaatcc	tagccgtggt	540
tatactaatt	acaatcagaa	gttcaaggac	cgcgtcacaa	tcactacaga	caaatccacc	600
agcacagcct	acatggaact	gagcagcctg	cgttctgagg	acactgcagt	ctattactgt	660
gcaagatatt	atgatgatca	ttactgcctt	gactactggg	gccaaggcac	cacggtcacc	720
gtctcctccg	gaggtggtgg	atccgagctc	gtgatgaccc	agactccact	ctccctgcct	780
gtcagtcttg	gagatcaagc	ctccatctct	tgcagatcta	gtcagagcct	tgtacacagt	840
aatggaaaca	cctatttaca	ttggtacctg	cagaagccag	gccagtctcc	aaagctcctg	900
atctacaaag	tttccaaccg	attttctggg	gtcccagaca	ggttcagtgg	cagtggatca	960
gggacagatt	tcacactcaa	gatcagcaga	gtggaggctg	aggatctggg	agttttatttc	1020
tgctctcaaa	gtacacatgt	tccgtacacg	ttcggagggg	ggaccaagct	tgagatcaaa	1080
ggtggtggtg	gttctggcgg	cggcggctcc	ggtggtggtg	gttctgaggt	gcagctgctc	1140
gagcagtctg	gagctgagct	ggcgaggcct	ggggcttcag	tgaagctgtc	ctgcaaggct	1200
tctggctaca	ccttcacaaa	ctatggttta	agctgggtga	agcagaggcc	tggacaggctc	1260
cttgagtgga	ttggagaggt	ttatcctaga	attggtaatg	cttactacaa	tgagaagttc	1320
aagggcaagg	ccacactgac	tgcagacaaa	tcctccagca	cagcgtccat	ggagctccgc	1380
agcctgacct	ctgaggactc	tgcggtctat	ttctgtgcaa	gacggggatc	ctacgatact	1440
aactacgact	ggtacttcga	tgtctggggc	caagggacca	cggtcaccgt	ctcctca	1497

<210> 307

<211> 499

<212> PRT

<213> artificial sequence

<220>

<223> VL1-VH7x4-7 LHLH

<400> 307

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Ser Tyr Met
20 25 30

Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr
35 40 45

Asp Thr Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
50 55 60

Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu
65 70 75 80

Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr
85 90 95

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Gly Glu Gly Thr Ser Thr
100 105 110

Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Val Gln Leu
115 120 125

Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val
130 135 140

~~Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp~~
145 150 155 160

Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn
165 170 175

Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe Lys Asp Arg Val
180 185 190

Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser
195 200 205

Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr²⁹⁷ Cys Ala Arg Tyr Tyr
 210 215 220

Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr
 225 230 235 240

Val Ser Ser Gly Gly Gly Gly Ser Glu Leu Val Met Thr Gln Thr Pro
 245 250 255

Leu Ser Leu Pro Val Ser Leu Gly Asp Gln Ala Ser Ile Ser Cys Arg
 260 265 270

Ser Ser Gln Ser Leu Val His Ser Asn Gly Asn Thr Tyr Leu His Trp
 275 280 285

Tyr Leu Gln Lys Pro Gly Gln Ser Pro Lys Leu Leu Ile Tyr Lys Val
 290 295 300

Ser Asn Arg Phe Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser
 305 310 315 320

Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu Asp Leu
 325 330 335

Gly Val Tyr Phe Cys Ser Gln Ser Thr His Val Pro Tyr Thr Phe Gly
 340 345 350

Gly Gly Thr Lys Leu Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly Gly
 355 360 365

Gly Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Leu Glu Gln Ser Gly
 370 375 380

Ala Glu Leu Ala Arg Pro Gly Ala Ser Val Lys Leu Ser Cys Lys Ala
 385 390 395 400

Ser Gly Tyr Thr Phe Thr Asn Tyr Gly Leu Ser Trp Val Lys Gln Arg
 405 410 415

Pro Gly Gln Val Leu Glu Trp Ile Gly Glu Val Tyr Pro Arg Ile Gly
 420 425 430

Asn Ala Tyr Tyr Asn Glu Lys Phe Lys Gly Lys Ala Thr Leu Thr Ala
 435 440 445

Asp Lys Ser Ser Ser Thr Ala Ser Met Glu Leu Arg Ser Leu Thr Ser
 450 455 460

Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg Arg Gly Ser Tyr Asp Thr
 465 470 475 480

Asn Tyr Asp Trp Tyr Phe Asp Val Trp Gly Gln Gly Thr Thr Val Thr

val Ser Ser

<210> 308

<211> 1500

<212> DNA

<213> artificial sequence

<220>

<223> VH7-VL1x4-7 HLLH

<400> 308

gacgtccaac tgggtgcagtc aggggctgaa gtgaaaaaac ctggggcctc agtgaagggtg	60
tcctgcaagg cttctggcta cacctttact aggtacacga tgcactgggt aaggcaggca	120
cctggacagg gtctggaatg gattggatac attaatccta gccgtgggta tactaattac	180
aatcagaagt tcaaggaccg cgtcacaatc actacagaca aatccaccag cacagcctac	240
atggaactga gcagcctgcg ttctgaggac actgcagtct attactgtgc aagatattat	300
gatgatcatt actgccttga ctactggggc caaggcacca cggtcaccgt ctcctcaggc	360
gaagggtacta gtactgggttc tgggtggaagt ggagggttcag gtggagcaga cgacattcag	420
atgacccagt ctccatctag cctgtctgca tctgtcgggg accgtgtcac catcacctgc	480
agagccagtc aaagtgtgtaag ttacatgaac tgggtaccagc agaagccggg caaggcaccc	540
aaaagatgga tttatgacac atccaaagtg gcttctggag tccctgctcg cttcagtggc	600
agtgggtctg ggaccgacta ctctctcaca atcaacagct tggaggctga agatgctgcc	660
acttattact gccaacagtg gagtagtaac ccgctcacgt tcggtggcgg gaccaagggtg	720
gagatcaaat ccggagggtg tggatccgag ctctgtgatga cccagactcc actctccctg	780
cctgtcagtc ttggagatca agcctccatc tcttgcagat ctagtcagag ccttgtagac	840
agtaatggaa acacctatctt acattgggtac ctgcagaagc caggccagtc tccaaagctc	900
ctgatctaca aagtttccaa ccgattttctt ggggtcccag acagggttcag tggcagtggg	960
tcagggacag atttcacact caagatcagc agagtggagg ctgaggatct gggagtatat	1020
ttctgctctc aaagtacaca tgttccgtac acgttcggag gggggaccaa gcttgagatc	1080
aaagggtggtg gtgggttctg cggcggcggc tccggtggtg gtgggttctga ggtgcagctg	1140
ctcgagcagt ctggagctga gctggcgagg cctggggctt cagtgaagct gtcctgcaag	1200
gcttctggct acaccttcac aaactatggt ttaagctggg tgaagcagag gcctggacag	1260
gtccttgagt ggattggaga ggtttatcct agaattggta atgcttacta caatgagaag	1320
ttcaagggca aggccacact gactgcagac aaatcctcca gcacagcgtc catggagctc	1380
cgcagcctga cctctgagga ctctgcggtc tatttctgtg caagacgggg atcctacgat	1440

actaactacg actggtactt cgatgtctgg ggccaaggga ccacgggtcac cgtctcctca 1500

<210> 309

<211> 500

<212> PRT

<213> artificial sequence

<220>

<223> VH7-VL1x4-7 HLLH

<400> 309

Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr
20 25 30

Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe
50 55 60

Lys Asp Arg Val Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly
115 120 125

Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Gln Met Thr Gln Ser
130 135 140

Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys
145 150 155 160

Arg Ala Ser Gln Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro
165 170 175

Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser
180 185 190

Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser

195	200	300	205
Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys			
210	215	220	
Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val			
225	230	235	240
Glu Ile Lys Ser Gly Gly Gly Gly Ser Glu Leu Val Met Thr Gln Thr			
	245	250	255
Pro Leu Ser Leu Pro Val Ser Leu Gly Asp Gln Ala Ser Ile Ser Cys			
	260	265	270
Arg Ser Ser Gln Ser Leu Val His Ser Asn Gly Asn Thr Tyr Leu His			
	275	280	285
Trp Tyr Leu Gln Lys Pro Gly Gln Ser Pro Lys Leu Leu Ile Tyr Lys			
	290	295	300
Val Ser Asn Arg Phe Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly			
305	310	315	320
Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu Asp			
	325	330	335
Leu Gly Val Tyr Phe Cys Ser Gln Ser Thr His Val Pro Tyr Thr Phe			
	340	345	350
Gly Gly Gly Thr Lys Leu Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly			
	355	360	365
Gly Gly Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Leu Glu Gln Ser			
	370	375	380
Gly Ala Glu Leu Ala Arg Pro Gly Ala Ser Val Lys Leu Ser Cys Lys			
385	390	395	400
Ala Ser Gly Tyr Thr Phe Thr Asn Tyr Gly Leu Ser Trp Val Lys Gln			
	405	410	415
Arg Pro Gly Gln Val Leu Glu Trp Ile Gly Glu Val Tyr Pro Arg Ile			
	420	425	430
Gly Asn Ala Tyr Tyr Asn Glu Lys Phe Lys Gly Lys Ala Thr Leu Thr			
	435	440	445
Ala Asp Lys Ser Ser Ser Thr Ala Ser Met Glu Leu Arg Ser Leu Thr			
	450	455	460
Ser Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg Arg Gly Ser Tyr Asp			
465	470	475	480

Thr Asn Tyr Asp Trp Tyr Phe Asp Val Trp Gly Gln Gly Thr Thr Val
 485 490 495

Thr Val Ser Ser
 500

<210> 310

<211> 1497

<212> DNA

<213> artificial sequence

<220>

<223> VL2VH7x4-7 LHL

<400> 310

gacattgtac	tgacccagtc	tccagcaact	ctgtctctgt	ctccagggga	gcgtgccacc	60
ctgagctgca	gagccagtca	aagtgttaagt	tacatgaact	ggtaccagca	gaagccgggc	120
aaggcaccca	aaagatggat	ttatgacaca	tccaaagtgg	cttctggagt	ccctgctcgc	180
ttcagtggca	gtgggtctgg	gaccgactac	tctctcacia	tcaacagctt	ggaggctgaa	240
gatgctgcca	cttattactg	ccaacagtgg	agtagtaacc	cgctcacgtt	cggtggcggg	300
accaaggtgg	agatcaaagg	cgaagggtact	agtactgggt	ctggtggaag	tggagggttca	360
ggtggagcag	acgacgtcca	actggtgcag	tcaggggctg	aagtgaaaaa	acctggggcc	420
tcagtgaagg	tgtcctgcaa	ggcttctggc	tacaccttta	ctaggtacac	gatgcactgg	480
gtaaggcagg	cacctggaca	gggtctggaa	tggattggat	acattaatcc	tagccgtggt	540
tatactaatt	acaatcagaa	gttcaaggac	cgcgtcacia	tcactacaga	caaatccacc	600
agcacagcct	acatggaact	gagcagcctg	cgttctgagg	acactgcagt	ctattactgt	660
gcaagatatt	atgatgatca	ttactgcctt	gactactggg	gccaaggcac	cacggtcacc	720
gtctcctccg	gaggtgggtg	atccgaggtg	cagctgctcg	agcagtctgg	agctgagctg	780
gcgaggcctg	gggcttcagt	gaagctgtcc	tgcaaggctt	ctggctacac	cttcacaaac	840
tatgggttta	gctgggtgaa	gcagaggcct	ggacagggtc	ttgagtggat	tggagagggt	900
tatcctagaa	ttggtaatgc	ttactacaat	gagaagttca	agggcaaggc	cacactgact	960
gcagacaaat	cctccagcac	agcgtccatg	gagctccgca	gcctgacctc	tgaggactct	1020
gcgggtctatt	tctgtgcaag	acggggatcc	tacgatacta	actacgactg	gtacttcgat	1080
gtctggggcc	aagggaccac	ggtcaccgtc	tcctcagggtg	gtgggtggttc	tggcggcggc	1140
ggctccgggtg	gtgggtggttc	tgagctcgtg	atgaccacaga	ctccactctc	cctgcctgtc	1200
agtcttggag	atcaagcctc	catctcttgc	agatctagtc	agagccttgt	acacagtaat	1260
ggaaacacct	atttacattg	gtacctgcag	aagccaggcc	agtctccaaa	gctcctgatc	1320

302

tacaaagttt ccaaccgatt ttctgggggtc ccagacaggt tcagtggcag tggatcaggg	1380
acagatttca cactcaagat cagcagagtg gaggctgagg atctgggagt ttatttctgc	1440
tctcaaagta cacatgttcc gtacacgttc ggagggggga ccaagcttga gatcaaa	1497

<210> 311
 <211> 499
 <212> PRT
 <213> artificial sequence

<220>

<223> VL2VH7x4-7 LHHL

<400> 311

Asp Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
 1 5 10 15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Tyr Met
 20 25 30

Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr
 35 40 45

Asp Thr Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
 50 55 60

Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu
 65 70 75 80

Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr
 85 90 95

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Gly Glu Gly Thr Ser Thr
 100 105 110

Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Val Gln Leu
 115 120 125

Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val
 130 135 140

Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp
 145 150 155 160

Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn
 165 170 175

Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe Lys Asp Arg Val
 180 185 190

Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser
 195 200 205
 Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Tyr Tyr
 210 215 220
 Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr
 225 230 240
 Val Ser Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Leu Glu Gln Ser
 245 250 255
 Gly Ala Glu Leu Ala Arg Pro Gly Ala Ser Val Lys Leu Ser Cys Lys
 260 265 270
 Ala Ser Gly Tyr Thr Phe Thr Asn Tyr Gly Leu Ser Trp Val Lys Gln
 275 280 285
 Arg Pro Gly Gln Val Leu Glu Trp Ile Gly Glu Val Tyr Pro Arg Ile
 290 295 300
 Gly Asn Ala Tyr Tyr Asn Glu Lys Phe Lys Gly Lys Ala Thr Leu Thr
 305 310 315 320
 Ala Asp Lys Ser Ser Ser Thr Ala Ser Met Glu Leu Arg Ser Leu Thr
 325 330 335
 Ser Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg Arg Gly Ser Tyr Asp
 340 345 350
 Thr Asn Tyr Asp Trp Tyr Phe Asp Val Trp Gly Gln Gly Thr Thr Val
 355 360 365
 Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
 370 375 380
 Gly Gly Ser Glu Leu Val Met Thr Gln Thr Pro Leu Ser Leu Pro Val
 385 390 395 400
 Ser Leu Gly Asp Gln Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu
 405 410 415
 Val His Ser Asn Gly Asn Thr Tyr Leu His Trp Tyr Leu Gln Lys Pro
 420 425 430
 Gly Gln Ser Pro Lys Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser
 435 440 445
 Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr
 450 455 460

Leu Lys Ile Ser Arg Val Glu Ala Glu Asp Leu Gly Val Tyr Phe Cys
 465 470 475 480

Ser Gln Ser Thr His Val Pro Tyr Thr Phe Gly Gly Gly Thr Lys Leu
 485 490 495

Glu Ile Lys

<210> 312

<211> 1500

<212> DNA

<213> artificial sequence

<220>

<223> VH7VL2x4-7 HLHL

<400> 312
 gacgtccaac tgggtgcagtc aggggctgaa gtgaaaaaac ctggggcctc agtgaagggtg 60
 tcctgcaagg cttctggcta cacctttact aggtacacga tgcactgggt aaggcaggca 120
 cctggacagg gtctggaatg gattggatac attaatccta gccgtgggta tactaattac 180
 aatcagaagt tcaaggaccg cgtcacaatc actacagaca aatccaccag cacagcctac 240
 atggaactga gcagcctgcg ttctgaggac actgcagtct attactgtgc aagatattat 300
 gatgatcatt actgccttga ctactggggc caaggcacca cggtcaccgt ctccctcaggc 360
 gaaggtacta gtactgggtc tgggtggaagt ggagggttcag gtggagcaga cgacattgta 420
 ctgacccagt ctccagcaac tctgtctctg tctccagggg agcgtgccac cctgagctgc 480
 agagccagtc aaagtgtaag ttacatgaac tgggtaccagc agaagccggg caaggcaccc 540
 aaaagatgga tttatgacac atccaaagtg gcttctggag tccctgctcg cttcagtggc 600
 agtgggtctg ggaccgacta ctctctcaca atcaacagct tggaggctga agatgctgcc 660
 acttattact gccaacagtg gagtagtaac ccgctcacgt tcggtggcgg gaccaagggtg 720
 gagatcaaat ccggagggtg tggatccgag gtgcagctgc tcgagcagtc tggagctgag 780
 ctggcgaggc ctggggcttc agtgaagctg tcctgcaagg cttctggcta caccttcaca 840
 aactatgggt taagctgggt gaagcagagg cctggacagg tccttgagtg gattggagag 900
 gtttatccta gaattggtaa tgcttactac aatgagaagt tcaagggcaa ggccacactg 960
 actgcagaca aatcctccag cacagcgtcc atggagctcc gcagcctgac ctctgaggac 1020
 tctgcggtct atttctgtgc aagacgggga tcctacgata ctaactacga ctggtacttc 1080
 gatgtctggg gccaagggac cacggtcacc gtctcctcag gtgggtgggtg ttctggcggc 1140
 ggcggctccg gtgggtgggtg ttctgagctc gtgatgaccc agactccact ctccctgcct 1200
 gtcagtcttg gagatcaagc ctccatctct tgcagatcta gtcagagcct tgtacacagt 1260

aatggaaaca cctattttaca ttggtacctg cagaagccag gccagtctcc aaagctcctg 1320
 atctacaaag tttccaaccg attttctggg gtcccagaca gggtcagtgg cagtggatca 1380
 gggacagatt tcacactcaa gatcagcaga gtggaggctg aggatctggg agtttatttc 1440
 tgctctcaaa gtacacatgt tccgtacacg ttcggagggg ggaccaagct tgagatcaaa 1500

<210> 313

<211> 500

<212> PRT

<213> artificial sequence

<220>

<223> VH7VL2x4-7 HLHL

<400> 313

Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
 1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr
 20 25 30

Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
 35 40 45

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe
 50 55 60

Lys Asp Arg Val Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr
 65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
 85 90 95

Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
 100 105 110

Thr Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly
 115 120 125

Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Val Leu Thr Gln Ser
 130 135 140

Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys
 145 150 155 160

Arg Ala Ser Gln Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro
 165 170 175

Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser
180 185 190

Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser
195 200 205

Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys
210 215 220

Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
225 230 235 240

Glu Ile Lys Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Leu Glu Gln
245 250 255

Ser Gly Ala Glu Leu Ala Arg Pro Gly Ala Ser Val Lys Leu Ser Cys
260 265 270

Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr Gly Leu Ser Trp Val Lys
275 280 285

Gln Arg Pro Gly Gln Val Leu Glu Trp Ile Gly Glu Val Tyr Pro Arg
290 295 300

Ile Gly Asn Ala Tyr Tyr Asn Glu Lys Phe Lys Gly Lys Ala Thr Leu
305 310 315 320

Thr Ala Asp Lys Ser Ser Ser Thr Ala Ser Met Glu Leu Arg Ser Leu
325 330 335

Thr Ser Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg Arg Gly Ser Tyr
340 345 350

Asp Thr Asn Tyr Asp Trp Tyr Phe Asp Val Trp Gly Gln Gly Thr Thr
355 360 365

Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
370 375 380

Gly Gly Gly Ser Glu Leu Val Met Thr Gln Thr Pro Leu Ser Leu Pro
385 390 395 400

Val Ser Leu Gly Asp Gln Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser
405 410 415

Leu Val His Ser Asn Gly Asn Thr Tyr Leu His Trp Tyr Leu Gln Lys
420 425 430

Pro Gly Gln Ser Pro Lys Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe
435 440 445

Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe
450 455 307 460

Thr Leu Lys Ile Ser Arg Val Glu Ala Glu Asp Leu Gly Val Tyr Phe
465 470 475 480

Cys Ser Gln Ser Thr His Val Pro Tyr Thr Phe Gly Gly Gly Thr Lys
485 490 495

Leu Glu Ile Lys
500

<210> 314

<211> 1497

<212> DNA

<213> artificial sequence

<220>

<223> VL2VH7x4-7 LHLH

<400> 314

gacattgtac	tgacccagtc	tccagcaact	ctgtctctgt	ctccagggga	gcgtgccacc	60
ctgagctgca	gagccagtca	aagtgttaagt	tacatgaact	ggtaccagca	gaagccgggc	120
aaggcaccca	aaagatggat	ttatgacaca	tccaaagtgg	cttctggagt	ccctgctcgc	180
ttcagtggca	gtgggtctgg	gaccgactac	tctctcacia	tcaacagctt	ggaggctgaa	240
gatgctgcca	cttattactg	ccaacagtgg	agtagtaacc	cgctcacgtt	cgggtggcggg	300
accaaggtgg	agatcaaagg	cgaagggtact	agtactgggt	ctggtggaag	tggagggttca	360
ggtggagcag	acgacgtcca	actggtgcag	tcaggggctg	aagtgaaaaa	acctgggggcc	420
tcagtgaagg	tgtcctgcaa	ggcttctggc	tacaccttta	ctagggtacac	gatgcactgg	480
gtaaggcagg	cacctggaca	gggtctggaa	tggattggat	acattaatcc	tagccgtggt	540
tatactaatt	acaatcagaa	gttcaaggac	cgcgtcacia	tcactacaga	caaatccacc	600
agcacagcct	acatggaact	gagcagcctg	cggttctgagg	acactgcagt	ctattactgt	660
gcaagatatt	atgatgatca	ttactgcctt	gactactggg	gccaaggcac	cacggtcacc	720
gtctcctccg	gaggtggtgg	atccgagctc	gtgatgaccc	agactccact	ctccctgcct	780
gtcagtcttg	gagatcaagc	ctccatctct	tgcagatcta	gtcagagcct	tgtacacagt	840
aatggaaaca	cctattttaca	ttggtacctg	cagaagccag	gccagtctcc	aaagctcctg	900
atctacaaag	tttccaaccg	atcttctggg	gtcccagaca	ggttcagtgg	cagtggatca	960
gggacagatt	tcacactcaa	gatcagcaga	gtggaggctg	aggatctggg	agttttatttc	1020
tgctctcaaa	gtacacatgt	tccgtacacg	ttcggagggg	ggaccaagct	tgagatcaaa	1080
ggtggtggtg	gttctggcgg	cggcgggtcc	ggtggtggtg	gttctgaggt	gcagctgctc	1140

308

gagcagtctg gagctgagct ggcgaggcct ggggcttcag tgaagctgtc ctgcaaggct	1200
tctggctaca ccttcacaaa ctatggttta agctgggtga agcagaggcc tggacaggct	1260
cttgagtgga ttggagaggt ttatcctaga attggtaatg cttactacaa tgagaagttc	1320
aagggcaagg ccacactgac tgcagacaaa tcctccagca cagcgtccat ggagctccgc	1380
agcctgacct ctgaggactc tgcggtctat ttctgtgcaa gacggggatc ctacgatact	1440
aactacgact ggtacttcga tgtctggggc caagggacca cggtcaccgt ctcctca	1497

<210> 315

<211> 499

<212> PRT

<213> artificial sequence

<220>

<223> VL2VH7x4-7 LHLH

<400> 315

Asp	Ile	Val	Leu	Thr	Gln	Ser	Pro	Ala	Thr	Leu	Ser	Leu	Ser	Pro	Gly
1				5					10					15	

Glu	Arg	Ala	Thr	Leu	Ser	Cys	Arg	Ala	Ser	Gln	Ser	Val	Ser	Tyr	Met
			20					25					30		

Asn	Trp	Tyr	Gln	Gln	Lys	Pro	Gly	Lys	Ala	Pro	Lys	Arg	Trp	Ile	Tyr
		35					40					45			

Asp	Thr	Ser	Lys	Val	Ala	Ser	Gly	Val	Pro	Ala	Arg	Phe	Ser	Gly	Ser
	50					55					60				

Gly	Ser	Gly	Thr	Asp	Tyr	Ser	Leu	Thr	Ile	Asn	Ser	Leu	Glu	Ala	Glu
65				70					75					80	

Asp	Ala	Ala	Thr	Tyr	Tyr	Cys	Gln	Gln	Trp	Ser	Ser	Asn	Pro	Leu	Thr
			85						90					95	

Phe	Gly	Gly	Gly	Thr	Lys	Val	Glu	Ile	Lys	Gly	Glu	Gly	Thr	Ser	Thr
			100					105					110		

Gly	Ser	Gly	Gly	Ser	Gly	Gly	Ser	Gly	Gly	Ala	Asp	Asp	Val	Gln	Leu
		115					120				125				

Val	Gln	Ser	Gly	Ala	Glu	Val	Lys	Lys	Pro	Gly	Ala	Ser	Val	Lys	Val
		130				135					140				

Ser	Cys	Lys	Ala	Ser	Gly	Tyr	Thr	Phe	Thr	Arg	Tyr	Thr	Met	His	Trp
145					150					155					160

Val Arg Gln Ala Pro Gly Gln Gly Leu Glu³⁰⁹ Trp Ile Gly Tyr Ile Asn
 165 170 175
 Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe Lys Asp Arg Val
 180 185 190
 Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser
 195 200 205
 Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Tyr Tyr
 210 215 220
 Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr
 225 230 235 240
 Val Ser Ser Gly Gly Gly Gly Ser Glu Leu Val Met Thr Gln Thr Pro
 245 250 255
 Leu Ser Leu Pro Val Ser Leu Gly Asp Gln Ala Ser Ile Ser Cys Arg
 260 265 270
 Ser Ser Gln Ser Leu Val His Ser Asn Gly Asn Thr Tyr Leu His Trp
 275 280 285
 Tyr Leu Gln Lys Pro Gly Gln Ser Pro Lys Leu Leu Ile Tyr Lys Val
 290 295 300
 Ser Asn Arg Phe Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser
 305 310 315 320
 Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu Asp Leu
 325 330 335
 Gly Val Tyr Phe Cys Ser Gln Ser Thr His Val Pro Tyr Thr Phe Gly
 340 345 350
 Gly Gly Thr Lys Leu Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly Gly
 355 360 365
 Gly Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Leu Glu Gln Ser Gly
 370 375 380
 Ala Glu Leu Ala Arg Pro Gly Ala Ser Val Lys Leu Ser Cys Lys Ala
 385 390 395 400
 Ser Gly Tyr Thr Phe Thr Asn Tyr Gly Leu Ser Trp Val Lys Gln Arg
 405 410 415
 Pro Gly Gln Val Leu Glu Trp Ile Gly Glu Val Tyr Pro Arg Ile Gly
 420 425 430
 Asn Ala Tyr Tyr Asn Glu Lys Phe Lys Gly Lys Ala Thr Leu Thr Ala

aaaggtggtg gtggttcttg cggcggcggc tccggtggtg gtggttctga ggtgcagctg 1140
 ctcgagcagt ctggagctga gctggcgagg cctggggcctt cagtgaagct gtcctgcaag 1200
 gcttctggct acaccttcac aaactatggt ttaagctggg tgaagcagag gcctggacag 1260
 gtccttgagt ggattggaga ggtttatcct agaattggta atgcttacta caatgagaag 1320
 ttcaagggca aggccacact gactgcagac aaatcctcca gcacagcgtc catggagctc 1380
 cgcagcctga cctctgagga ctctgcggtc tatttctgtg caagacgggg atcctacgat 1440
 actaactacg actggtactt cgatgtctgg ggccaaggga ccacggtcac cgtctcctca 1500

<210> 317

<211> 500

<212> PRT

<213> artificial sequence

<220>

<223> VH7VL2x4-7 HLLH

<400> 317

Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
 1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr
 20 25 30

Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
 35 40 45

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe
 50 55 60

Lys Asp Arg Val Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr
 65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
 85 90 95

Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
 100 105 110

Thr Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly
 115 120 125

Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Val Leu Thr Gln Ser
 130 135 140

Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys

145		150		312 155		160
Arg Ala Ser Gln	Ser Val	Ser Tyr Met	Asn Trp Tyr Gln Gln	Lys	Pro	
	165		170	175		
Gly Lys Ala Pro	Lys Arg Trp Ile	Tyr Asp Thr Ser	Lys Val	Ala Ser		
	180	185	190			
Gly Val Pro	Ala Arg Phe Ser	Gly Ser Gly Ser	Gly Thr	Asp Tyr Ser		
	195	200	205			
Leu Thr Ile	Asn Ser Leu	Glu Ala Glu Asp	Ala Thr	Tyr Tyr Cys		
	210	215	220			
Gln Gln Trp Ser	Ser Asn Pro	Leu Thr Phe	Gly Gly Gly Thr	Lys Val		
	225	230	235	240		
Glu Ile Lys Ser	Gly Gly Gly Gly	Ser Glu	Leu Val Met Thr	Gln Thr		
	245	250		255		
Pro Leu Ser	Leu Pro Val	Ser Leu Gly	Asp Gln Ala Ser	Ile Ser Cys		
	260	265	270			
Arg Ser Ser	Gln Ser Leu Val	His Ser Asn Gly	Asn Thr Tyr	Leu His		
	275	280	285			
Trp Tyr Leu	Gln Lys Pro	Gly Gln Ser Pro	Lys Leu Leu Ile Tyr	Lys		
	290	295	300			
Val Ser Asn	Arg Phe Ser	Gly Val Pro Asp	Arg Phe Ser Gly	Ser Gly		
	305	310	315	320		
Ser Gly Thr Asp	Phe Thr Leu Lys	Ile Ser Arg Val	Glu Ala Glu Asp			
	325	330	335			
Leu Gly Val Tyr	Phe Cys Ser Gln	Ser Thr His Val	Pro Tyr Thr Phe			
	340	345	350			
Gly Gly Gly Thr	Lys Leu Glu Ile	Lys Gly Gly Gly	Gly Ser Gly Gly			
	355	360	365			
Gly Gly Ser Gly	Gly Gly Gly Gly	Ser Glu Val Gln	Leu Leu Glu Gln Ser			
	370	375	380			
Gly Ala Glu Leu	Ala Arg Pro Gly	Ala Ser Val Lys	Leu Ser Cys Lys			
	385	390	395	400		
Ala Ser Gly Tyr	Thr Phe Thr Asn Tyr	Gly Leu Ser Trp	Val Lys Gln			
	405	410	415			
Arg Pro Gly Gln	Val Leu Glu Trp Ile	Gly Glu Val Tyr	Pro Arg Ile			
	420	425	430			

Gly Asn Ala Tyr Tyr Asn Glu Lys Phe Lys Gly Lys Ala Thr Leu Thr
 435 440 445

Ala Asp Lys Ser Ser Ser Thr Ala Ser Met Glu Leu Arg Ser Leu Thr
 450 455 460

Ser Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg Arg Gly Ser Tyr Asp
 465 470 475 480

Thr Asn Tyr Asp Trp Tyr Phe Asp Val Trp Gly Gln Gly Thr Thr Val
 485 490 495

Thr Val Ser Ser
 500

<210> 318

<211> 1497

<212> DNA

<213> artificial sequence

<220>

<223> VL3VH7x4-7 LHHL

<400> 318

gacattgtac tgaccagtc tccagcaact ctgtctctgt ctccagggga gcgtgccacc	60
ctgacctgca gagccagttc aagtgtaagt tacatgaact ggtaccagca gaagccgggc	120
aaggcaccga aaagatggat ttatgacaca tccaaagtgg cttctggagt ccctgctcgc	180
ttcagtggca gtgggtctgg gaccgactac tctctcaca tcaacagctt ggaggctgaa	240
gatgctgcca cttattactg ccaacagtgg agtagtaacc cgctcacgtt cggtggcggg	300
accaaggtgg agatcaaagg cgaaggtact agtactgggt ctggtggaag tggagggttca	360
ggtggagcag acgacgtcca actggtgcag tcaggggctg aagtgaaaaa acctggggcc	420
tcagtgaagg tgtcctgcaa ggcttctggc tacaccttta ctaggtacac gatgcactgg	480
gtaaggcagg cacctggaca gggctctggaa tggattggat acattaatcc tagccgtggt	540
tatactaatt acaatcagaa gttcaaggac cgcgtcaca tcactacaga caaatccacc	600
agcacagcct acatggaact gagcagcctg cgttctgagg aactgcagt ctattactgt	660
gcaagatatt atgatgatca ttactgcctt gactactggg gccaaaggcac cacggtcacc	720
gtctcctccg gaggtgggtg atccgaggtg cagctgctcg agcagtctgg agctgagctg	780
gcgaggcctg gggcttcagt gaagctgtcc tgcaaggctt ctggctacac cttcacaac	840
tatggtttaa gctgggtgaa gcagaggcct ggacaggtcc ttgagtggat tggagaggtt	900
tatcctagaa ttggtaatgc ttactacaat gagaagttca agggcaaggc cacactgact	960

314

gcagacaaat cctccagcac agcgtccatg gagctccgca gcctgacctc tgaggactct	1020
gcggtctatt tctgtgcaag acgggggatcc tacgatacta actacgactg gtacttcgat	1080
gtctggggcc aagggaccac ggtcaccgtc tcctcaggtg gtggtgggtc tggcggcggc	1140
ggctccggtg gtggtgggtc tgagctcgtg atgacccaga ctccactctc cctgcctgtc	1200
agtcttgag atcaagcctc catctcttgc agatctagtc agagccttgt acacagtaat	1260
ggaaacacct atttacattg gtacctgcag aagccaggcc agtctccaaa gctcctgatc	1320
tacaaagttt ccaaccgatt ttctggggtc ccagacaggt tcagtggcag tggatcaggg	1380
acagatttca cactcaagat cagcagagtg gaggctgagg atctgggagt ttatttctgc	1440
tctcaaagta cacatgttcc gtacacgttc ggagggggga ccaagcttga gatcaaa	1497

<210> 319

<211> 499

<212> PRT

<213> artificial sequence

<220>

<223> VL3VH7x4-7 LHHL

<400> 319

Asp Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
1 5 10 15

Glu Arg Ala Thr Leu Thr Cys Arg Ala Ser Ser Ser Val Ser Tyr Met
20 25 30

Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr
35 40 45

Asp Thr Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
50 55 60

Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu
65 70 75 80

Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr
85 90 95

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Gly Glu Gly Thr Ser Thr
100 105 110

Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Val Gln Leu
115 120 125

Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val
130 135 140

Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp
 145 150 155 160
 Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn
 165 170 175
 Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe Lys Asp Arg Val
 180 185 190
 Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser
 195 200 205
 Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Tyr Tyr
 210 215 220
 Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr
 225 230 235 240
 Val Ser Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Leu Glu Gln Ser
 245 250 255
 Gly Ala Glu Leu Ala Arg Pro Gly Ala Ser Val Lys Leu Ser Cys Lys
 260 265 270
 Ala Ser Gly Tyr Thr Phe Thr Asn Tyr Gly Leu Ser Trp Val Lys Gln
 275 280 285
 Arg Pro Gly Gln Val Leu Glu Trp Ile Gly Glu Val Tyr Pro Arg Ile
 290 295 300
 Gly Asn Ala Tyr Tyr Asn Glu Lys Phe Lys Gly Lys Ala Thr Leu Thr
 305 310 315 320
 Ala Asp Lys Ser Ser Ser Thr Ala Ser Met Glu Leu Arg Ser Leu Thr
 325 330 335
 Ser Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg Arg Gly Ser Tyr Asp
 340 345 350
 Thr Asn Tyr Asp Trp Tyr Phe Asp Val Trp Gly Gln Gly Thr Thr Val
 355 360 365
 Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
 370 375 380
 Gly Gly Ser Glu Leu Val Met Thr Gln Thr Pro Leu Ser Leu Pro Val
 385 390 395 400
 Ser Leu Gly Asp Gln Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu
 405 410 415

Val His Ser Asn Gly Asn Thr Tyr Leu His Trp Tyr Leu Gln Lys Pro
 420 425 430

Gly Gln Ser Pro Lys Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser
 435 440 445

Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr
 450 455 460

Leu Lys Ile Ser Arg Val Glu Ala Glu Asp Leu Gly Val Tyr Phe Cys
 465 470 475 480

Ser Gln Ser Thr His Val Pro Tyr Thr Phe Gly Gly Gly Thr Lys Leu
 485 490 495

Glu Ile Lys

<210> 320

<211> 1500

<212> DNA

<213> artificial sequence

<220>

<223> VH7VL3x4-7 HLHL

<400> 320
 gacgtccaac tgggtgcagtc aggggctgaa gtgaaaaaac ctggggcctc agtgaagggtg 60
 tcctgcaagg cttctggcta cacctttact aggtacacga tgcactgggt aaggcaggca 120
 cctggacagg gtctggaatg gattggatac attaatccta gccgtgggtta tactaattac 180
 aatcagaagt tcaaggaccg cgtcacaatc actacagaca aatccaccag cacagcctac 240
 atggaactga gcagcctgcg ttctgaggac actgcagtct attactgtgc aagatattat 300
 gatgatcatt actgccttga ctactggggc caaggcacca cggtcaccgt ctcttcaggc 360
 gaaggtacta gtactgggttc tgggtggaagt ggagggttcag gtggagcaga cgacattgta 420
 ctgacccagt ctccagcaac tctgtctctg tctccagggg agcgtgccac cctgacctgc 480
 agagccagtt caagtgtaag ttacatgaac tgggtaccagc agaagccggg caaggcaccc 540
 aaaagatgga tttatgacac atccaaagtg gcttctggag tccctgctcg cttcagtggc 600
 agtgggtctg ggaccgacta ctctctcaca atcaacagct tggaggctga agatgctgcc 660
 acttattact gccaacagtg gagtagtaac ccgctcacgt tcggtggcgg gaccaagggtg 720
 gagatcaa at ccggagggtg tggatccgag gtgcagctgc tcgagcagtc tggagctgag 780
 ctggcgaggc ctggggcttc agtgaagctg tcctgcaagg cttctggcta caccttcaca 840
 aactatggtt taagctgggt gaagcagagg cctggacagg tccttgagtg gattggagag 900

gtttatccta gaattggtâa tgcttactac aatgagaagt tcaagggcaa ggccacactg 960
 actgcagaca aatcctccag cacagcgtcc atggagctcc gcagcctgac ctctgaggac 1020
 tctgcggtct atttctgtgc aagacgggga tcctacgata ctaactacga ctggtacttc 1080
 gatgtctggg gccaagggac cacggtcacc gtctcctcag gtggtggtgg ttctggcggc 1140
 ggcggctccg gtggtggtgg ttctgagctc gtgatgaccc agactccact ctccctgcct 1200
 gtcagtcttg gagatcaagc ctccatctct tgcagatcta gtcagagcct tgtacacagt 1260
 aatggaaaca cctattttaca ttggtacctg cagaagccag gccagtctcc aaagctcctg 1320
 atctacaaag tttccaaccg attttctggg gtcccagaca gggttcagtgg cagtggatca 1380
 gggacagatt tcacactcaa gatcagcaga gtggaggctg aggatctggg agttttatttc 1440
 tgctctcaaa gtacacatgt tccgtacacg ttcggagggg ggaccaagct tgagatcaaa 1500

<210> 321

<211> 500

<212> PRT

<213> artificial sequence

<220>

<223> VH7VL3x4-7 HLHL

<400> 321

Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr
20 25 30

Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe
50 55 60

Lys Asp Arg Val Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly
115 120 125

Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Val Leu Thr Gln Ser
130 135 140

Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Thr Cys
145 150 155 160

Arg Ala Ser Ser Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro
165 170 175

Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser
180 185 190

Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser
195 200 205

Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys
210 215 220

Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
225 230 235 240

Glu Ile Lys Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Leu Glu Gln
245 250 255

Ser Gly Ala Glu Leu Ala Arg Pro Gly Ala Ser Val Lys Leu Ser Cys
260 265 270

Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr Gly Leu Ser Trp Val Lys
275 280 285

Gln Arg Pro Gly Gln Val Leu Glu Trp Ile Gly Glu Val Tyr Pro Arg
290 295 300

Ile Gly Asn Ala Tyr Tyr Asn Glu Lys Phe Lys Gly Lys Ala Thr Leu
305 310 315 320

Thr Ala Asp Lys Ser Ser Ser Thr Ala Ser Met Glu Leu Arg Ser Leu
325 330 335

Thr Ser Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg Arg Gly Ser Tyr
340 345 350

Asp Thr Asn Tyr Asp Trp Tyr Phe Asp Val Trp Gly Gln Gly Thr Thr
355 360 365

Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
370 375 380

Gly Gly Gly Ser Glu Leu Val Met Thr Gln Thr Pro Leu Ser Leu Pro
385 390 395 400

val Ser Leu Gly Asp Gln Ala Ser Ile Ser³¹⁹ Cys Arg Ser Ser Gln Ser
 405 410 415
 Leu Val His Ser Asn Gly Asn Thr Tyr Leu His Trp Tyr Leu Gln Lys
 420 425 430
 Pro Gly Gln Ser Pro Lys Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe
 435 440 445
 Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe
 450 455 460
 Thr Leu Lys Ile Ser Arg Val Glu Ala Glu Asp Leu Gly Val Tyr Phe
 465 470 475 480
 Cys Ser Gln Ser Thr His Val Pro Tyr Thr Phe Gly Gly Gly Thr Lys
 485 490 495
 Leu Glu Ile Lys
 500

<210> 322

<211> 1497

<212> DNA

<213> artificial sequence

<220>

<223> VL3VH7x4-7 LHLH

<400> 322

gacattgtac tgacccagtc tccagcaact ctgtctctgt ctccagggga gcgtgccacc	60
ctgacctgca gagccagttc aagtgttaagt tacatgaact ggtaccagca gaagccgggc	120
aaggcaccga aaagatggat ttatgacaca tccaaagtgg cttctggagt ccctgctcgc	180
ttcagtggca gtgggtctgg gaccgactac tctctcaca tcaacagctt ggaggctgaa	240
gatgctgcca cttattactg ccaacagtgg agtagtaacc cgctcacgtt cggtggcggg	300
accaaggtgg agatcaaagg cgaaggtact agtactgggt ctggtggaag tggaggttca	360
ggtggagcag acgacgtcca actggtgcag tcaggggctg aagtgaaaaa acctggggcc	420
tcagtgaagg tgtcctgcaa ggcttctggc tacaccttta ctaggtacac gatgcactgg	480
gtaaggcagg cacctggaca gggctctggaa tggattggat acattaatcc tagccgtggt	540
tatactaatt acaatcagaa gttcaaggac cgcgtcaca tcactacaga caaatccacc	600
agcacagcct acatggaact gagcagcctg cgttctgagg aactgcagt ctattactgt	660
gcaagatatt atgatgatca ttactgcctt gactactggg gccaaaggcac cacggtcacc	720
gtctcctccg gaggtgggtgg atccgagctc gtgatgaccc agactccact ctccctgcct	780

320

gtcagtcttg gagatcaagc ctccatctct tgcagatcta gtcagagcct tgtacacagt	840
aatggaaaca cctatttaca ttggtacctg cagaagccag gccagtctcc aaagctcctg	900
atctacaaag tttccaaccg attttctggg gtcccagaca ggttcagtgg cagtggatca	960
gggacagatt tcacactcaa gatcagcaga gtggaggctg aggatctggg agtttatttc	1020
tgctctcaaa gtacacatgt tccgtacacg ttcggagggg ggaccaagct tgagatcaaa	1080
ggtggtggtg gttctggcgg cggcggctcc ggtggtggtg gttctgaggt gcagctgctc	1140
gagcagtctg gagctgagct ggcgaggcct ggggcttcag tgaagctgtc ctgcaaggct	1200
tctggctaca ccttcacaaa ctatggttta agctgggtga agcagaggcc tggacaggctc	1260
cttgagtgga ttggagaggt ttatcctaga attggtaatg cttactacaa tgagaagttc	1320
aagggcaagg ccacactgac tgcagacaaa tcctccagca cagcgtccat ggagctccgc	1380
agcctgacct ctgaggactc tgcggtctat ttctgtgcaa gacggggatc ctacgatact	1440
aactacgact ggtacttcga tgtctggggc caagggacca cggtcaccgt ctcctca	1497

<210> 323

<211> 499

<212> PRT

<213> artificial sequence

<220>

<223> VL3VH7x4-7 LHLH

<400> 323

Asp Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
1 5 10 15

Glu Arg Ala Thr Leu Thr Cys Arg Ala Ser Ser Ser Val Ser Tyr Met
20 25 30

Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr
35 40 45

Asp Thr Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
50 55 60

Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu
65 70 75 80

Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr
85 90 95

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Gly Glu Gly Thr ser Thr
100 105 110

Gly ser Gly Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp val Gln Leu
 115 120 321 125
 val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val
 130 135 140
 Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp
 145 150 155 160
 Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn
 165 170 175
 Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe Lys Asp Arg Val
 180 185 190
 Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser
 195 200 205
 Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Tyr Tyr
 210 215 220
 Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr
 225 230 235 240
 Val Ser Ser Gly Gly Gly Gly Ser Glu Leu Val Met Thr Gln Thr Pro
 245 250 255
 Leu Ser Leu Pro Val Ser Leu Gly Asp Gln Ala Ser Ile Ser Cys Arg
 260 265 270
 Ser Ser Gln Ser Leu Val His Ser Asn Gly Asn Thr Tyr Leu His Trp
 275 280 285
 Tyr Leu Gln Lys Pro Gly Gln Ser Pro Lys Leu Leu Ile Tyr Lys Val
 290 295 300
 Ser Asn Arg Phe Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser
 305 310 315 320
 Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu Asp Leu
 325 330 335
 Gly Val Tyr Phe Cys Ser Gln Ser Thr His Val Pro Tyr Thr Phe Gly
 340 345 350
 Gly Gly Thr Lys Leu Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly Gly
 355 360 365
 Gly Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Leu Glu Gln Ser Gly
 370 375 380
 Ala Glu Leu Ala Arg Pro Gly Ala Ser Val Lys Leu Ser Cys Lys Ala

385		390		322 395		400
ser Gly Tyr Thr Phe Thr Asn Tyr Gly Leu Ser Trp val Lys Gln Arg				410		415
		405				
Pro Gly Gln val Leu Glu Trp Ile Gly Glu val Tyr Pro Arg Ile Gly				425		430
		420				
Asn Ala Tyr Tyr Asn Glu Lys Phe Lys Gly Lys Ala Thr Leu Thr Ala				440		445
		435				
Asp Lys Ser Ser Ser Thr Ala Ser Met Glu Leu Arg Ser Leu Thr Ser				455		460
		450				
Glu Asp Ser Ala val Tyr Phe Cys Ala Arg Arg Gly Ser Tyr Asp Thr				470		475
		465				480
Asn Tyr Asp Trp Tyr Phe Asp val Trp Gly Gln Gly Thr Thr val Thr				485		490
		485				495

val ser ser

<210> 324

<211> 1500

<212> DNA

<213> artificial sequence

<220>

<223> VH7VL3x4-7 HLLH

<400> 324

gacgtccaac tgggtgcagtc aggggctgaa gtgaaaaaac ctggggcctc agtgaagggtg	60
tcctgcaagg cttctggcta cacctttact aggtacacga tgcactgggt aaggcaggca	120
cctggacagg gtctggaatg gattggatac attaatccta gccgtgggta tactaattac	180
aatcagaagt tcaaggaccg cgtcacaatc actacagaca aatccaccag cacagcctac	240
atggaactga gcagcctgcg ttctgaggac actgcagtct attactgtgc aagatattat	300
gatgatcatt actgccttga ctactggggc caaggcacca cggtcacctg ctcctcaggc	360
gaagg tacta gtactgggtc tgggtggaagt ggagggttcag gtggagcaga cgacattgta	420
ctgacccagt ctccagcaac tctgtctctg tctccagggg agcgtgccac cctgacctgc	480
agagccagtt caagtgtaag ttacatgaac tgggtaccagc agaagccggg caaggcacc	540
aaaagatgga tttatgacac atccaaagtg gcttctggag tccctgctcg cttcagtggc	600
agtgggtctg ggaccgacta ctctctcaca atcaacagct tggaggctga agatgctgcc	660
acttattact gccaacagtg gagtagtaac ccgctcacgt tcgggtggcg gaccaagggtg	720

gagatcaaat ccggaggtgg tggatccgag ctcgtgatga cccagactcc actctccctg 780
 cctgtcagtc ttggagatca agcctccatc tcttgcagat ctagtcagag ccttgtacac 840
 agtaatggaa acacctatattt acattggtac ctgcagaagc caggccagtc tccaaagctc 900
 ctgatctaca aagtttccaa ccgattttct ggggtcccag acaggttcag tggcagtgga 960
 tcagggacag atttcacact caagatcagc agagtggagg ctgaggatct gggagtttat 1020
 ttctgctctc aaagtacaca tgttccgtac acgttcggag gggggaccaa gcttgagatc 1080
 aaagggtggtg gtggttctgg cggcggcggc tccggtggtg gtggttctga ggtgcagctg 1140
 ctcgagcagt ctggagctga gctggcgagg cctggggctt cagtgaagct gtcctgcaag 1200
 gcttctggct acaccttcac aaactatggt ttaagctggg tgaagcagag gcctggacag 1260
 gtccttgagt ggattggaga ggtttatcct agaattggta atgcttacta caatgagaag 1320
 ttcaagggca aggccacact gactgcagac aaatcctcca gcacagcgtc catggagctc 1380
 cgcagcctga cctctgagga ctctgcggtc tatttctgtg caagacgggg atcctacgat 1440
 actaactacg actggtactt cgatgtctgg ggccaagggg ccacggtcac cgtctcctca 1500

<210> 325

<211> 500

<212> PRT

<213> artificial sequence

<220>

<223> VH7VL3x4-7 HLLH

<400> 325

Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr
20 25 30

Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe
50 55 60

Lys Asp Arg Val Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly

[illegible]

325

Gly Ala Glu Leu Ala Arg Pro Gly Ala Ser Val Lys Leu Ser Cys Lys
385 390 395 400

Ala Ser Gly Tyr Thr Phe Thr Asn Tyr Gly Leu Ser Trp Val Lys Gln
405 410 415

Arg Pro Gly Gln Val Leu Glu Trp Ile Gly Glu Val Tyr Pro Arg Ile
420 425 430

Gly Asn Ala Tyr Tyr Asn Glu Lys Phe Lys Gly Lys Ala Thr Leu Thr
435 440 445

Ala Asp Lys Ser Ser Ser Thr Ala Ser Met Glu Leu Arg Ser Leu Thr
450 455 460

Ser Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg Arg Gly Ser Tyr Asp
465 470 475 480

Thr Asn Tyr Asp Trp Tyr Phe Asp Val Trp Gly Gln Gly Thr Thr Val
485 490 495

Thr Val Ser Ser
500

<210> 326

<211> 1494

<212> DNA

<213> artificial sequence

<220>

<223> VL1VH5xCD19 LHHL

<400> 326

gacattcaga tgacccagtc tccatctagc ctgtctgcat ctgtcgggga ccgtgtcacc	60
atcacctgca gagccagtca aagtgttaagt tacatgaact ggtaccagca gaagccgggc	120
aaggcaccga aaagatggat ttatgacaca tccaaagtgg cttctggagt ccctgctcgc	180
ttcagtggca gtgggtctgg gaccgactac tctctcaca tcaacagctt ggaggctgaa	240
gatgctgcca cttattactg ccaacagtgg agtagtaacc cgctcacgtt cgggtggcggg	300
accaaggtgg agatcaaagg cgaaggtact agtactgggt ctggtggaag tggaggttca	360
gggtggagcag acgacgtcca actggtgcag tcaggggctg aagtgaaaaa acctggggcc	420
tcagtgaagg tgtcctgcaa ggcttctggc tacaccttta ctaggtacac gatgcactgg	480
gtaaggcagg cacctggaca gggctctggaa tggattggat acattaatcc tagccgtggt	540
tatactaatt acgcagacag cgtcaagggc cgcttcacaa tcactacaga caaatccacc	600

326

agcacagcct acatggaact gagcagcctg cgttctgagg acactgcaac ctattactgt	660
gcaagatatt atgatgatca ttactgcctt gactactggg gccaaaggcac cacggtcacc	720
gtctcctccg gaggtggtgg atcccagggtg cagctgcagc agtctggggc tgagctggtg	780
aggcctgggt cctcagtga gatttcctgc aaggcttctg gctatgcatt cagtagctac	840
tggatgaact ggggtgaagca gaggcctgga caggggtcttg agtggattgg acagatttgg	900
cctggagatg gtgatactaa ctacaatgga aagttcaagg gtaaagccac tctgactgca	960
gacgaatcct ccagcacagc ctacatgcaa ctcagcagcc tagcatctga ggactctgcg	1020
gtctatttct gtgcaagacg ggagactacg acggtaggcc gttattacta tgctatggac	1080
tactggggcc aagggaccac ggtcaccgtc tcctccggtg gtggtggttc tggcggcggc	1140
ggctccggtg gtggtggttc tgatatccag ctgacccagt ctccagcttc tttggctgtg	1200
tctctagggc agagggccac catctcctgc aaggccagcc aaagtgttga ttatgatggt	1260
gatagttatt tgaactggta ccaacagatt ccaggacagc cacccaaact cctcatctat	1320
gatgcatcca atctagtttc tgggatccca cccaggttta gtggcagtgg gtctgggaca	1380
gacttcaccc tcaacatcca tcctgtggag aagggtggatg ctgcaaccta tcaactgtcag	1440
caaagtactg aggatccgtg gacgttcggt ggagggacca agctcgagat caaa	1494

<210> 327

<211> 498

<212> PRT

<213> artificial sequence

<220>

<223> VL1VH5xCD19 LHHL

<400> 327

Asp	Ile	Gln	Met	Thr	Gln	Ser	Pro	Ser	Ser	Leu	Ser	Ala	Ser	Val	Gly
1				5				10						15	

Asp	Arg	Val	Thr	Ile	Thr	Cys	Arg	Ala	Ser	Gln	Ser	Val	Ser	Tyr	Met
			20					25					30		

Asn	Trp	Tyr	Gln	Gln	Lys	Pro	Gly	Lys	Ala	Pro	Lys	Arg	Trp	Ile	Tyr
		35					40					45			

Asp	Thr	Ser	Lys	Val	Ala	Ser	Gly	Val	Pro	Ala	Arg	Phe	Ser	Gly	Ser
	50					55					60				

Gly	Ser	Gly	Thr	Asp	Tyr	Ser	Leu	Thr	Ile	Asn	Ser	Leu	Glu	Ala	Glu
65				70						75					80

Asp	Ala	Ala	Thr	Tyr	Tyr	Cys	Gln	Gln	Trp	Ser	Ser	Asn	Pro	Leu	Thr
				85					90					95	

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Gly Glu Gly Thr Ser Thr
 100 105 110
 Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Val Gln Leu
 115 120 125
 Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val
 130 135 140
 Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp
 145 150 155 160
 Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn
 165 170 175
 Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val Lys Gly Arg Phe
 180 185 190
 Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser
 195 200 205
 Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys Ala Arg Tyr Tyr
 210 215 220
 Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr
 225 230 235 240
 Val Ser Ser Gly Gly Gly Gly Ser Gln Val Gln Leu Gln Gln Ser Gly
 245 250 255
 Ala Glu Leu Val Arg Pro Gly Ser Ser Val Lys Ile Ser Cys Lys Ala
 260 265 270
 Ser Gly Tyr Ala Phe Ser Ser Tyr Trp Met Asn Trp Val Lys Gln Arg
 275 280 285
 Pro Gly Gln Gly Leu Glu Trp Ile Gly Gln Ile Trp Pro Gly Asp Gly
 290 295 300
 Asp Thr Asn Tyr Asn Gly Lys Phe Lys Gly Lys Ala Thr Leu Thr Ala
 305 310 315 320
 Asp Glu Ser Ser Ser Thr Ala Tyr Met Gln Leu Ser Ser Leu Ala Ser
 325 330 335
 Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg Arg Glu Thr Thr Thr Val
 340 345 350
 Gly Arg Tyr Tyr Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Thr Val
 355 360 365

328

Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
370 375 380

Gly Gly Ser Asp Ile Gln Leu Thr Gln Ser Pro Ala Ser Leu Ala Val
385 390 395 400

Ser Leu Gly Gln Arg Ala Thr Ile Ser Cys Lys Ala Ser Gln Ser Val
405 410 415

Asp Tyr Asp Gly Asp Ser Tyr Leu Asn Trp Tyr Gln Gln Ile Pro Gly
420 425 430

Gln Pro Pro Lys Leu Leu Ile Tyr Asp Ala Ser Asn Leu Val Ser Gly
435 440 445

Ile Pro Pro Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu
450 455 460

Asn Ile His Pro Val Glu Lys Val Asp Ala Ala Thr Tyr His Cys Gln
465 470 475 480

Gln Ser Thr Glu Asp Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu Glu
485 490 495

Ile Lys

<210> 328

<211> 1497

<212> DNA

<213> artificial sequence

<220>

<223> VH5VL1xCD19 HLHL

<400> 328
gacgtccaac tgggtgcagtc aggggctgaa gtgaaaaaac ctggggcctc agtgaagggtg 60
tcctgcaagg cttctggcta cacctttact aggtacacga tgcactgggt aaggcaggca 120
cctggacagg gtctggaatg gattggatac attaatccta gccgtgggtta tactaattac 180
gcagacagcg tcaagggccg cttcacaatc actacagaca aatccaccag cacagcctac 240
atggaactga gcagcctgcg ttctgaggac actgcaacct attactgtgc aagatattat 300
gatgatcatt actgccttga ctactggggc caaggcacca cggtcaccgt ctctcaggc 360
gaaggtacta gtactgggtc tgggtggaagt ggaggttcag gtggagcaga cgacattcag 420
atgacccagt ctccatctag cctgtctgca tctgtcgggg accgtgtcac catcacctgc 480
agagccagtc aaagtgtaag ttacatgaac tgggtaccagc agaagccggg caaggcaccc 540

aaaagatgga tttatgacac atccaaagtg gcttctggag tccctgctcg cttcagtggc 600
 agtgggtctg ggaccgacta ctctctcaca atcaacagct tggaggctga agatgctgcc 660
 acttattact gccaacagtg gagtagtaac ccgctcacgt tcggtggcgg gaccaaggtg 720
 gagatcaa at cccggaggtg tggatcccag gtgcagctgc agcagtctgg ggctgagctg 780
 gtgaggcctg ggtcctcagt gaagatttcc tgcaaggctt ctggctatgc attcagtagc 840
 tactggatga actgggtgaa gcagaggcct ggacaggggc ttgagtggat tggacagatt 900
 tggcctggag atggtgatac taactacaat ggaaagttca agggtaaagc cactctgact 960
 gcagacgaat cctccagcac agcctacatg caactcagca gcctagcatc tgaggactct 1020
 gcggtctatt tctgtgcaag acgggagact acgacggtag gccgttatta ctatgctatg 1080
 gactactggg gccaagggac cacggtcacc gtctcctccg gtggtggtgg ttctggcggc 1140
 ggcggctccg gtggtggtgg ttctgatatc cagctgaccc agtctccagc ttctttggct 1200
 gtgtctctag ggcagagggc caccatctcc tgcaaggcca gccaaagtgt tgattatgat 1260
 ggtgatagtt atttgaactg gtaccaacag attccaggac agccacccaa actcctcatc 1320
 tatgatgcat ccaatctagt ttctgggatc ccaccaggt ttagtggcag tgggtctggg 1380
 acagacttca ccctcaacat ccctcctgtg gagaagggtg atgctgcaac ctatcactgt 1440
 cagcaaagta ctgaggatcc gtggacgttc ggtggaggga ccaagctcga gatcaaa 1497

<210> 329

<211> 499

<212> PRT

<213> artificial sequence

<220>

<223> VH5VL1xCD19 HLHL

<400> 329

Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
 1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr
 20 25 30

Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
 35 40 45

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val
 50 55 60

Lys Gly Arg Phe Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr
 65 70 75 80

Met Glu Leu Ser Ser₈₅ Leu Arg Ser Glu Asp₉₀ Thr Ala Thr Tyr Tyr₉₅ Cys

Ala Arg Tyr Tyr₁₀₀ Asp Asp His Tyr Cys₁₀₅ Leu Asp Tyr Trp Gly₁₁₀ Gln Gly

Thr Thr Val₁₁₅ Thr Val Ser Ser Gly₁₂₀ Glu Gly Thr Ser Thr₁₂₅ Gly Ser Gly

Gly Ser₁₃₀ Gly Gly Ser Gly₁₃₅ Ala Asp Asp Ile Gln₁₄₀ Met Thr Gln Ser

Pro Ser Ser Leu Ser Ala₁₅₀ Ser Val Gly Asp Arg₁₅₅ Val Thr Ile Thr Cys₁₆₀

Arg Ala Ser Gln Ser₁₆₅ Val Ser Tyr Met Asn₁₇₀ Trp Tyr Gln Gln Lys₁₇₅ Pro

Gly Lys Ala Pro₁₈₀ Lys Arg Trp Ile Tyr₁₈₅ Asp Thr Ser Lys Val₁₉₀ Ala Ser

Gly Val Pro₁₉₅ Ala Arg Phe Ser Gly₂₀₀ Ser Gly Ser Gly Thr₂₀₅ Asp Tyr Ser

Leu Thr Ile Asn Ser Leu Glu₂₁₅ Ala Glu Asp Ala Ala₂₂₀ Thr Tyr Tyr Cys

Gln Gln Trp Ser Ser Asn₂₃₀ Pro Leu Thr Phe Gly₂₃₅ Gly Gly Thr Lys Val₂₄₀

Glu Ile Lys Ser Gly₂₄₅ Gly Gly Gly Ser Gln₂₅₀ Val Gln Leu Gln Gln₂₅₅ Ser

Gly Ala Glu Leu₂₆₀ Val Arg Pro Gly Ser₂₆₅ Ser Val Lys Ile Ser₂₇₀ Cys Lys

Ala Ser Gly Tyr Ala Phe Ser Ser Tyr Trp Met Asn₂₈₅ Trp Val Lys Gln

Arg Pro Gly Gln Gly Leu Glu₂₉₅ Trp Ile Gly Gln Ile Trp Pro Gly Asp

Gly Asp Thr Asn Tyr Asn Gly Lys Phe Lys Gly₃₁₅ Lys Ala Thr Leu Thr₃₂₀

Ala Asp Glu Ser Ser₃₂₅ Ser Thr Ala Tyr Met₃₃₀ Gln Leu Ser Ser Leu Ala₃₃₅

ser Glu Asp Ser Ala Val Tyr Phe Cys₃₄₅ Ala Arg Arg Glu Thr₃₅₀ Thr Thr

val Gly Arg Tyr Tyr Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Thr
 355 360 331 365
 val Thr val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
 370 375 380
 Gly Gly Gly Ser Asp Ile Gln Leu Thr Gln Ser Pro Ala Ser Leu Ala
 385 390 395 400
 val Ser Leu Gly Gln Arg Ala Thr Ile Ser Cys Lys Ala Ser Gln Ser
 405 410 415
 val Asp Tyr Asp Gly Asp Ser Tyr Leu Asn Trp Tyr Gln Gln Ile Pro
 420 425 430
 Gly Gln Pro Pro Lys Leu Leu Ile Tyr Asp Ala Ser Asn Leu Val Ser
 435 440 445
 Gly Ile Pro Pro Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr
 450 455 460
 Leu Asn Ile His Pro Val Glu Lys Val Asp Ala Ala Thr Tyr His Cys
 465 470 475 480
 Gln Gln Ser Thr Glu Asp Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu
 485 490 495

Glu Ile Lys

<210> 330

<211> 1494

<212> DNA

<213> artificial sequence

<220>

<223> VL1VH5xCD19 LHLH

<400> 330

gacattcaga tgaccagtc tccatctagc ctgtctgcat ctgtcgggga ccgtgtcacc	60
atcacctgca gagccagtca aagtgtgaagt tacatgaact ggtaccagca gaagccgggc	120
aaggcaccga aaagatggat ttatgacaca tccaaagtgg cttctggagt ccctgctcgc	180
ttcagtggca gtgggtctgg gaccgactac tctctcacia tcaacagctt ggaggctgaa	240
gatgctgcca cttattactg ccaacagtgg agtagtaacc cgctcacgtt cggtggcggg	300
accaaggtgg agatcaaagg cgaaggtact agtactgggt ctggtggaag tggaggttca	360
ggtggagcag acgacgtcca actggtgcag tcaggggctg aagtgaaaaa acctggggcc	420

332

tcagtgaagg tgtcctgcaa ggcttctggc tacaccttta ctaggtacac gatgcactgg	480
gtaaggcagg cacctggaca gggctctggaa tggattggat acattaatcc tagccgtggg	540
tatactaatt acgcagacag cgtcaagggc cgcttcacaa tcactacaga caaatccacc	600
agcacagcct acatggaact gagcagcctg cgcttctgagg aactgcaac ctattactgt	660
gcaagatatt atgatgatca ttactgcctt gactactggg gccaaaggcac cacggtcacc	720
gtctcctccg gaggtgggtg atccgatatc cagctgaccc agtctccagc ttctttggct	780
gtgtctctag ggcagagggc caccatctcc tgcaaggcca gccaaagtgt tgattatgat	840
ggatgatagtt atttgaactg gtaccaacag attccaggac agccacccaa actcctcatc	900
tatgatgcat ccaatctagt ttctgggatc ccaccaggt ttagtggcag tgggtctggg	960
acagacttca ccctcaacat ccctcctgtg gagaagggtg atgctgcaac ctatcactgt	1020
cagcaaagta ctgaggatcc gtggacgttc ggtggaggga ccaagctcga gatcaaaggt	1080
gggtgggtgt ctggcggcgg cggtccgggt ggtgggtggt ctcagggtgca gctgcagcag	1140
tctggggctg agctgggtgag gcctgggtcc tcagtgaaga tttcctgcaa ggcttctggc	1200
tatgcattca gtagctactg gatgaactgg gtgaagcaga ggcttggaac gggctcttgag	1260
tggattggac agatttggtc tggagatggg gatactaact acaatggaaa gttcaagggt	1320
aaagccactc tgactgcaga cgaatcctcc agcacagcct acatgcaact cagcagccta	1380
gcatctgagg actctgcggt ctatttctgt gcaagacggg agactacgac ggtaggccgt	1440
tattactatg ctatggacta ctggggccaa gggaccacgg tcaccgtctc ctcc	1494

<210> 331

<211> 498

<212> PRT

<213> artificial sequence

<220>

<223> VL1VH5xCD19 LHLH

<400> 331

----- Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly -----
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Ser Tyr Met
20 25 30

Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr
35 40 45

Asp Thr Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
50 55 60

Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile³³³ Asn Ser Leu Glu Ala Glu
 65 70 75 80
 Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr
 85 90 95
 Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Gly Glu Gly Thr Ser Thr
 100 105 110
 Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Val Gln Leu
 115 120 125
 Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val
 130 135 140
 Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp
 145 150 155 160
 Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn
 165 170 175
 Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val Lys Gly Arg Phe
 180 185 190
 Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser
 195 200 205
 Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys Ala Arg Tyr Tyr
 210 215 220
 Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr
 225 230 235 240
 Val Ser Ser Gly Gly Gly Gly Ser Asp Ile Gln Leu Thr Gln Ser Pro
 245 250 255
 Ala Ser Leu Ala Val Ser Leu Gly Gln Arg Ala Thr Ile Ser Cys Lys
 260 265 270
 Ala Ser Gln Ser Val Asp Tyr Asp Gly Asp Ser Tyr Leu Asn Trp Tyr
 275 280 285
 Gln Gln Ile Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr Asp Ala Ser
 290 295 300
 Asn Leu Val Ser Gly Ile Pro Pro Arg Phe Ser Gly Ser Gly Ser Gly
 305 310 315 320
 Thr Asp Phe Thr Leu Asn Ile His Pro Val Glu Lys Val Asp Ala Ala
 325 330 335
 Thr Tyr His Cys Gln Gln Ser Thr Glu Asp Pro Trp Thr Phe Gly Gly

gaaggtacta gtactggttc tgggtggaagt ggaggttcag gtggagcaga cgacattcag 420
 atgacccagt ctccatctag cctgtctgca tctgtcgggg accgtgtcac catcacctgc 480
 agagccagtc aaagtgtaag ttacatgaac tgggtaccagc agaagccggg caaggcaccc 540
 aaaagatgga tttatgacac atccaaagtg gcttctggag tccctgctcg cttcagtggc 600
 agtgggtctg ggaccgacta ctctctcaca atcaacagct tggaggctga agatgctgcc 660
 acttattact gccaacagtg gagtagtaac ccgctcacgt tcggtggcgg gaccaaggtg 720
 gagatcaaat ccggaggtgg tggatccgat atccagctga cccagtctcc agcttctttg 780
 gctgtgtctc tagggcagag ggccaccatc tcctgcaagg ccagccaaag tgttgattat 840
 gatggtgata gttatttgaa ctggtaccaa cagattccag gacagccacc caaactcctc 900
 atctatgatg catccaatct agtttctggg atcccacca ggtttagtgg cagtgggtct 960
 gggacagact tcaccctcaa catccatcct gtggagaagg tggatgctgc aacctatcac 1020
 tgtcagcaaa gtactgagga tccgtggacg ttcggtggag ggaccaagct cgagatcaaa 1080
 ggtggtggtg gttctggcgg cggcggctcc ggtggtggtg gttctcaggt gcagctgcag 1140
 cagtctgggg ctgagctggt gaggcctggg tcctcagtga agatttcctg caaggcttct 1200
 ggctatgcat tcagtagcta ctggatgaac tgggtgaagc agaggcctgg acagggtctt 1260
 gagtggattg gacagatttg gcctggagat ggtgatacta actacaatgg aaagttcaag 1320
 ggtaaagcca ctctgactgc agacgaatcc tccagcacag cctacatgca actcagcagc 1380
 ctagcatctg aggactctgc ggtctatttc tgtgcaagac gggagactac gacggtaggc 1440
 cgttattact atgctatgga ctactggggc caagggacca cggtcaccgt ctctcc 1497

<210> 333

<211> 499

<212> PRT

<213> artificial sequence

<220>

<223> VH5VL1xCD19 HLLH

<400> 333

Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
 1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr
 20 25 30

Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
 35 40 45

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val

50 55 336 60
 Lys Gly Arg Phe Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr
 65 70 75 80
 Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys
 85 90 95
 Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
 100 105 110
 Thr Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly
 115 120 125
 Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Gln Met Thr Gln Ser
 130 135 140
 Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys
 145 150 155 160
 Arg Ala Ser Gln Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro
 165 170 175
 Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser
 180 185 190
 Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser
 195 200 205
 Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys
 210 215 220
 Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
 225 230 235 240
 Glu Ile Lys Ser Gly Gly Gly Gly Ser Asp Ile Gln Leu Thr Gln Ser
 245 250 255
 Pro Ala Ser Leu Ala Val Ser Leu Gly Gln Arg Ala Thr Ile Ser Cys
 260 265 270
 Lys Ala Ser Gln Ser Val Asp Tyr Asp Gly Asp Ser Tyr Leu Asn Trp
 275 280 285
 Tyr Gln Gln Ile Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr Asp Ala
 290 295 300
 Ser Asn Leu Val Ser Gly Ile Pro Pro Arg Phe Ser Gly Ser Gly Ser
 305 310 315 320
 Gly Thr Asp Phe Thr Leu Asn Ile His Pro Val Glu Lys Val Asp Ala
 325 330 335

Ala Thr Tyr His Cys Gln Gln Ser Thr Glu Asp Pro Trp Thr Phe Gly
 340 345 350

Gly Gly Thr Lys Leu Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly Gly
 355 360 365

Gly Ser Gly Gly Gly Gly Ser Gln Val Gln Leu Gln Gln Ser Gly Ala
 370 375 380

Glu Leu Val Arg Pro Gly Ser Ser Val Lys Ile Ser Cys Lys Ala Ser
 385 390 395 400

Gly Tyr Ala Phe Ser Ser Tyr Trp Met Asn Trp Val Lys Gln Arg Pro
 405 410 415

Gly Gln Gly Leu Glu Trp Ile Gly Gln Ile Trp Pro Gly Asp Gly Asp
 420 425 430

Thr Asn Tyr Asn Gly Lys Phe Lys Gly Lys Ala Thr Leu Thr Ala Asp
 435 440 445

Glu Ser Ser Ser Thr Ala Tyr Met Gln Leu Ser Ser Leu Ala Ser Glu
 450 455 460

Asp Ser Ala Val Tyr Phe Cys Ala Arg Arg Glu Thr Thr Thr Val Gly
 465 470 475 480

Arg Tyr Tyr Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr
 485 490 495

Val Ser Ser

<210> 334

<211> 1494

<212> DNA

<213> artificial sequence

<220>

<223> VL2/VH5xCD19 LHHL

<400> 334

gacattgtac tgaccagtc tccagcaact ctgtctctgt ctccagggga gcgtgccacc	60
ctgagctgca gagccagtca aagtgtaagt tacatgaact ggtaccagca gaagccgggc	120
aaggcaccca aaagatggat ttatgacaca tccaaagtgg cttctggagt ccctgctcgc	180
ttcagtggca gtgggtctgg gaccgactac tctctcaca tcaacagctt ggaggctgaa	240

338

gatgctgcca cttattactg ccaacagtgg agtagtaacc cgctcacgtt cgggtggcggg	300
accaaggtgg agatcaaagg cgaaggtact agtactgggt ctggtggaag tggagggttca	360
gggtggagcag acgacgtcca actggtgcag tcaggggctg aagtgaaaaa acctggggcc	420
tcagtgaagg tgtcctgcaa ggcttctggc tacaccttta ctaggtacac gatgcactgg	480
gtaaggcagg cacctggaca gggctctggaa tggattggat acattaatcc tagccgtggg	540
tatactaatt acgcagacag cgtcaagggc cgcttcacaa tcactacaga caaatccacc	600
agcacagcct acatggaact gagcagcctg cgttctgagg aactgcaac ctattactgt	660
gcaagatatt atgatgatca ttactgcctt gactactggg gccaaggcac cacggtcacc	720
gtctcctccg gaggtgggtg atcccagggt cagctgcagc agtctggggc tgagctgggtg	780
aggcctgggt cctcagtga gatttcctgc aaggcttctg gctatgcatt cagtagctac	840
tggatgaact ggggtgaagca gaggcctgga cagggtcttg agtggattgg acagatttgg	900
cctggagatg gtgatactaa ctacaatgga aagttcaagg gtaaagccac tctgactgca	960
gacgaatcct ccagcacagc ctacatgcaa ctcagcagcc tagcatctga ggactctgcg	1020
gtctatttct gtgcaagacg ggagactacg acggtaggcc gttattacta tgctatggac	1080
tactggggcc aagggaccac ggtcaccgtc tcctccgggtg gtgggtgggtt tggcggcggc	1140
ggctccgggtg gtgggtgggtt tgatatccag ctgaccagct ctccagcttc tttggctgtg	1200
tctctagggc agagggccac catctcctgc aaggccagcc aaagtgttga ttatgatggg	1260
gatagttatt tgaactggta ccaacagatt ccaggacagc caccctaaact cctcatctat	1320
gatgcatcca atctagtttc tgggatccca cccaggttta gtggcagtgg gtctggggaca	1380
gacttcaccc tcaacatcca tcctgtggag aagggtggatg ctgcaaccta tcactgtcag	1440
caaagtactg aggatccgtg gacgttcggt ggagggacca agctcgagat caaa	1494

<210> 335

<211> 498

<212> PRT

<213> artificial sequence

<220>

<223> VL2/VH5xCD19 LHHL

<400> 335

Asp	Ile	Val	Leu	Thr	Gln	Ser	Pro	Ala	Thr	Leu	Ser	Leu	Ser	Pro	Gly
1				5					10					15	

Glu	Arg	Ala	Thr	Leu	Ser	Cys	Arg	Ala	Ser	Gln	Ser	Val	Ser	Tyr	Met
			20					25					30		

Asn	Trp	Tyr	Gln	Gln	Lys	Pro	Gly	Lys	Ala	Pro	Lys	Arg	Trp	Ile	Tyr
		35					40					45			

Asp Thr Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
 50 55 60
 Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu
 65 70 75 80
 Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr
 85 90 95
 Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Gly Glu Gly Thr Ser Thr
 100 105 110
 Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Val Gln Leu
 115 120 125
 Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val
 130 135 140
 Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp
 145 150 155 160
 Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn
 165 170 175
 Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val Lys Gly Arg Phe
 180 185 190
 Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser
 195 200 205
 Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys Ala Arg Tyr Tyr
 210 215 220
 Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr
 225 230 235 240
 Val Ser Ser Gly Gly Gly Gly Ser Gln Val Gln Leu Gln Gln Ser Gly
 245 250 255
 Ala Glu Leu Val Arg Pro Gly Ser Ser Val Lys Ile Ser Cys Lys Ala
 260 265 270
 Ser Gly Tyr Ala Phe Ser Ser Tyr Trp Met Asn Trp Val Lys Gln Arg
 275 280 285
 Pro Gly Gln Gly Leu Glu Trp Ile Gly Gln Ile Trp Pro Gly Asp Gly
 290 295 300
 Asp Thr Asn Tyr Asn Gly Lys Phe Lys Gly Lys Ala Thr Leu Thr Ala
 305 310 315 320

340

Asp Glu Ser Ser Ser Thr Ala Tyr Met Gln Leu Ser Ser Leu Ala Ser
325 330 335

Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg Arg Glu Thr Thr Thr Val
340 345 350

Gly Arg Tyr Tyr Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Thr Val
355 360 365

Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly
370 375 380

Gly Gly Ser Asp Ile Gln Leu Thr Gln Ser Pro Ala Ser Leu Ala Val
385 390 395 400

Ser Leu Gly Gln Arg Ala Thr Ile Ser Cys Lys Ala Ser Gln Ser Val
405 410 415

Asp Tyr Asp Gly Asp Ser Tyr Leu Asn Trp Tyr Gln Gln Ile Pro Gly
420 425 430

Gln Pro Pro Lys Leu Leu Ile Tyr Asp Ala Ser Asn Leu Val Ser Gly
435 440 445

Ile Pro Pro Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu
450 455 460

Asn Ile His Pro Val Glu Lys Val Asp Ala Ala Thr Tyr His Cys Gln
465 470 475 480

Gln Ser Thr Glu Asp Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu Glu
485 490 495

Ile Lys

<210> 336

<211> 1497

<212> DNA

<213> artificial sequence

<220>

<223> VH5VL2xCD19 HLHL

<400> 336
gacgtccaac tgggtgcagtc aggggctgaa gtgaaaaaac ctggggcctc agtgaagggtg 60
tcctgcaagg cttctggcta cacctttact aggtacacga tgcactgggt aaggcaggca 120
cctggacagg gtctggaatg gattggatac attaatccta gccgtgggta tactaattac 180

gcagacagcg tcaagggccg cttcacaaatc actacagaca aatccaccag cacagcctac 240
atggaactga gcagcctgcg ttctgaggac actgcaacct attactgtgc aagatattat 300
gatgatcatt actgccttga ctactggggc caaggcacca cggtcaccgt ctcctcaggc 360
gaagg tacta gtactgggttc tgggtggaagt ggagggttcag gtggagcaga cgacattgta 420
ctgacccagt ctccagcaac tctgtctctg tctccagggg agcgtgccac cctgagctgc 480
agagccagtc aaagtgtaag ttacatgaac tgggtaccagc agaagccggg caaggcaccc 540
aaaagatgga tttatgacac atccaaagtg gcttctggag tccctgctcg cttcagtggc 600
agtgggtctg ggaccgacta ctctctcaca atcaacagct tggaggctga agatgctgcc 660
acttattact gccaacagtg gagtagtaac ccgctcacgt tcgggtggcg gaccaagggtg 720
gagatcaaat ccggagggtg tggatcccag gtgcagctgc agcagtctgg ggctgagctg 780
gtgaggcctg ggtcctcagt gaagatttcc tgcaaggctt ctggctatgc attcagtagc 840
tactggatga actgggtgaa gcagaggcct ggacagggtc ttgagtggat tggacagatt 900
tggcctggag atgggtgatac taactacaat ggaaagtcca agggtaaagc cactctgact 960
gcagacgaat cctccagcac agcctacatg caactcagca gcctagcatc tgaggactct 1020
gcggtctatt tctgtgcaag acgggagact acgacggtag gccgttatta ctatgctatg 1080
gactactggg gccaaaggac cacggtcacc gtctcctccg gtgggtgggtg ttctggcggc 1140
ggcggctccg gtgggtgggtg ttctgatatac cagctgaccc agtctccagc ttctttggct 1200
gtgtctctag ggcagagggc caccatctcc tgcaaggcca gccaaagtgt tgattatgat 1260
ggatgatgtt atttgaactg gtaccaacag attccaggac agccacccaa actcctcatc 1320
tatgatgat ccaatctagt ttctgggatc ccaccagggt ttagtggcag tgggtctggg 1380
acagacttca ccctcaacat ccattcctgtg gagaagggtg atgctgcaac ctatcactgt 1440
cagcaaagta ctgaggatcc gtggacgttc ggtggaggga ccaagctcga gatcaaa 1497

<210> 337

<211> 499

<212> PRT

<213> artificial sequence

<220>

<223> VH5VL2xCD19 HLHL

<400> 337

Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr
20 25 30

Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
 35 40 45

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val
 50 55 60

Lys Gly Arg Phe Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr
 65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys
 85 90 95

Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
 100 105 110

Thr Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly
 115 120 125

Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Val Leu Thr Gln Ser
 130 135 140

Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys
 145 150 155 160

Arg Ala Ser Gln Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro
 165 170 175

Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser
 180 185 190

Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser
 195 200 205

Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys
 210 215 220

Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
 225 230 235 240

~~Glu Ile Lys Ser Gly Gly Gly Gly Ser Gln Val Gln Leu Gln Gln Ser~~
 245 250 255

Gly Ala Glu Leu Val Arg Pro Gly Ser Ser Val Lys Ile Ser Cys Lys
 260 265 270

Ala Ser Gly Tyr Ala Phe Ser Ser Tyr Trp Met Asn Trp Val Lys Gln
 275 280 285

Arg Pro Gly Gln Gly Leu Glu Trp Ile Gly Gln Ile Trp Pro Gly Asp
 290 295 300

Gly Asp Thr Asn Tyr Asn Gly Lys Phe Lys Gly Lys Ala Thr Leu Thr
305 310 315 343 320

Ala Asp Glu Ser Ser Ser Thr Ala Tyr Met Gln Leu Ser Ser Leu Ala
325 330 335

Ser Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg Arg Glu Thr Thr Thr
340 345 350

Val Gly Arg Tyr Tyr Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Thr
355 360 365

Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Ser Gly
370 375 380

Gly Gly Gly Ser Asp Ile Gln Leu Thr Gln Ser Pro Ala Ser Leu Ala
385 390 395 400

Val Ser Leu Gly Gln Arg Ala Thr Ile Ser Cys Lys Ala Ser Gln Ser
405 410 415

Val Asp Tyr Asp Gly Asp Ser Tyr Leu Asn Trp Tyr Gln Gln Ile Pro
420 425 430

Gly Gln Pro Pro Lys Leu Leu Ile Tyr Asp Ala Ser Asn Leu Val Ser
435 440 445

Gly Ile Pro Pro Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr
450 455 460

Leu Asn Ile His Pro Val Glu Lys Val Asp Ala Ala Thr Tyr His Cys
465 470 475 480

Gln Gln Ser Thr Glu Asp Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu
485 490 495

Glu Ile Lys

<210> 338

<211> 1494

<212> DNA

<213> artificial sequence

<220>

<223> VL2/VH5xCD19

<400> 338

gacattgtac tgacccagtc tccagcaact ctgtctctgt ctccagggga gcgtgccacc

344

ctgagctgca gagccagtca aagtgtgaagt tacatgaact ggtaccagca gaagccgggc	120
aaggcacca aaagatggat ttatgacaca tccaaagtgg cttctggagt ccctgctcgc	180
ttcagtggca gtgggtcttg gaccgactac tctctcacia tcaacagctt ggaggctgaa	240
gatgctgcca cttattactg ccaacagtgg agtagtaacc cgctcacgtt cggtggcggg	300
accaaggtgg agatcaaagg cgaagggtact agtactgggt ctggtggaag tggagggttca	360
ggtggagcag acgacgtcca actggtgcag tcaggggctg aagtgaaaaa acctggggcc	420
tcagtgaagg tgtcctgcaa ggcttctggc tacaccttta ctaggtacac gatgcactgg	480
gtaaggcagg cacctggaca gggctctggaa tggattggat acattaatcc tagccgtggg	540
tatactaatt acgcagacag cgtcaagggc cgcttcacia tcactacaga caaatccacc	600
agcacagcct acatggaact gagcagcctg cgcttctgagg aactgcaac ctattactgt	660
gcaagatatt atgatgatca ttactgcctt gactactggg gccaaaggcac cacggtcacc	720
gtctcctccg gaggtgggtg atccgatatc cagctgaccc agtctccagc ttctttggct	780
gtgtctctag ggcagagggc caccatctcc tgcaaggcca gccaaagtgt tgattatgat	840
ggtgatagtt atttgaactg gtaccaacag attccaggac agccacccaa actcctcatc	900
tatgatgcat ccaatctagt ttctgggac ccacccaggt ttagtggcag tgggtctggg	960
acagacttca ccctcaacat ccacctctgt gagaagggtg atgctgcaac ctatcactgt	1020
cagcaaagta ctgaggatcc gtggacgttc ggtggaggga ccaagctcga gatcaaaggt	1080
ggtgggtgggt ctggcggcgg cggtccgggt ggtgggtgggt ctcagggtgca gctgcagcag	1140
tctggggctg agctgggtgag gcctgggtcc tcagtgaaga tttcctgcaa ggcttctggc	1200
tatgcattca gtagctactg gatgaactgg gtgaagcaga ggcctggaca gggctcttgag	1260
tggattggac agatttggcc tggagatggg gatactaact acaatggaaa gttcaagggt	1320
aaagccactc tgactgcaga cgaatcctcc agcacagcct acatgcaact cagcagccta	1380
gcattctgagg actctgcgggt ctatttctgt gcaagacggg agactacgac ggtaggccgt	1440
tattactatg ctatggacta ctggggccaa gggaccacgg tcaccgtctc ctcc	1494

<210> 339

<211> 498

<212> PRT

<213> artificial sequence

<220>

<223> VL2/VH5xCD19

<400> 339

Asp	Ile	Val	Leu	Thr	Gln	Ser	Pro	Ala	Thr	Leu	Ser	Leu	Ser	Pro	Gly
1				5					10					15	

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser³⁴⁵ Gln Ser Val Ser Tyr Met
 20 25 30

Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr
 35 40 45

Asp Thr Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
 50 55 60

Gly ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu
 65 70 75 80

Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr
 85 90 95

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Gly Glu Gly Thr Ser Thr
 100 105 110

Gly ser Gly Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Val Gln Leu
 115 120 125

Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val
 130 135 140

Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp
 145 150 155 160

Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn
 165 170 175

Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val Lys Gly Arg Phe
 180 185 190

Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser
 195 200 205

Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys Ala Arg Tyr Tyr
 210 215 220

Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr
 225 230 235 240

Val Ser Ser Gly Gly Gly Gly Ser Asp Ile Gln Leu Thr Gln Ser Pro
 245 250 255

Ala Ser Leu Ala Val Ser Leu Gly Gln Arg Ala Thr Ile Ser Cys Lys
 260 265 270

Ala Ser Gln Ser Val Asp Tyr Asp Gly Asp Ser Tyr Leu Asn Trp Tyr
 275 280 285

Gln Gln Ile Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr Asp Ala Ser

290 295 346 300
 Asn Leu Val Ser Gly Ile Pro Pro Arg Phe Ser Gly Ser Gly Ser Gly
 305 310 315 320
 Thr Asp Phe Thr Leu Asn Ile His Pro Val Glu Lys Val Asp Ala Ala
 325 330 335
 Thr Tyr His Cys Gln Gln Ser Thr Glu Asp Pro Trp Thr Phe Gly Gly
 340 345 350
 Gly Thr Lys Leu Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly
 355 360 365
 Ser Gly Gly Gly Gly Ser Gln Val Gln Leu Gln Gln Ser Gly Ala Glu
 370 375 380
 Leu Val Arg Pro Gly Ser Ser Val Lys Ile Ser Cys Lys Ala Ser Gly
 385 390 395 400
 Tyr Ala Phe Ser Ser Tyr Trp Met Asn Trp Val Lys Gln Arg Pro Gly
 405 410 415
 Gln Gly Leu Glu Trp Ile Gly Gln Ile Trp Pro Gly Asp Gly Asp Thr
 420 425 430
 Asn Tyr Asn Gly Lys Phe Lys Gly Lys Ala Thr Leu Thr Ala Asp Glu
 435 440 445
 Ser Ser Ser Thr Ala Tyr Met Gln Leu Ser Ser Leu Ala Ser Glu Asp
 450 455 460
 Ser Ala Val Tyr Phe Cys Ala Arg Arg Glu Thr Thr Thr Val Gly Arg
 465 470 475 480
 Tyr Tyr Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val
 485 490 495
 Ser Ser

<210> 340

<211> 1497

<212> DNA

<213> artificial sequence

<220>

<223> VH5VL2xCD19 HLLH

<400> 340

gacgtccaac	tggtgcagtc	aggggctgaa	gtgaaaaaac	ctggggcctc	agtgaagggtg	60
tcctgcaagg	cttctggcta	cacctttact	aggtacacga	tgcactgggt	aaggcaggca	120
cctggacagg	gtctggaatg	gattggatac	attaatccta	gccgtggtta	tactaattac	180
gcagacagcg	tcaagggccg	cttcacaatc	actacagaca	aatccaccag	cacagcctac	240
atggaactga	gcagcctgcg	ttctgaggac	actgcaacct	attactgtgc	aagatattat	300
gatgatcatt	actgccttga	ctactggggc	caaggcacca	cggtcaccgt	ctcctcaggc	360
gaagggtacta	gtactgggtc	tggtggaagt	ggagggttcag	gtggagcaga	cgacattgta	420
ctgacccagt	ctccagcaac	tctgtctctg	tctccagggg	agcgtgccac	cctgagctgc	480
agagccagtc	aaagtgtaag	ttacatgaac	tggtaccagc	agaagccggg	caaggcaccc	540
aaaagatgga	tttatgacac	atccaaagtg	gcttctggag	tccctgctcg	cttcagtggc	600
agtgggtctg	ggaccgacta	ctctctcaca	atcaacagct	tggaggctga	agatgctgcc	660
acttattact	gccaacagtg	gagtagtaac	ccgctcacgt	tcggtggcgg	gaccaagggtg	720
gagatcaaata	ccggagggtg	tggatccgat	atccagctga	cccagtctcc	agcttctttg	780
gctgtgtctc	tagggcagag	ggccaccatc	tcctgcaagg	ccagccaaag	tgttgattat	840
gatggtgata	gttatttgaa	ctggtaccaa	cagattccag	gacagccacc	caaactcctc	900
atctatgatg	catccaatct	agtttctggg	atcccaccca	ggtttagtg	cagtgggtct	960
gggacagact	tcaccctcaa	catccatcct	gtggagaagg	tggatgctgc	aacctatcac	1020
tgtcagcaaa	gtactgagga	tccgtggacg	ttcgggtggag	ggaccaagct	cgagatcaaa	1080
gggtgggtg	gttctggcgg	cggcggctcc	gggtgggtg	gttctcagg	gcagctgcag	1140
cagtctgggg	ctgagctggt	gaggcctggg	tcctcagtga	agatttcctg	caaggcttct	1200
ggctatgcat	tcagtagcta	ctggatgaac	tgggtgaagc	agaggcctgg	acagggtctt	1260
gagtggattg	gacagatttg	gcctggagat	ggtgatacta	actacaatgg	aaagttcaag	1320
ggtaaagcca	ctctgactgc	agacgaatcc	tccagcacag	cctacatgca	actcagcagc	1380
ctagcatctg	aggactctgc	ggtctatttc	tgtgcaagac	gggagactac	gacggtaggc	1440
cgttattact	atgctatgga	ctactggggc	caagggacca	cggtcaccgt	ctcctcc	1497

<210> 341

<211> 499

<212> PRT

<213> artificial sequence

<220>

<223> VH5VL2xCD19 HLLH

<400> 341

Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala

1	5	10	348	15
Ser	Val	Lys	Val	Ser
			20	
Cys	Lys	Ala	Ser	Gly
			25	
Tyr	Thr	Phe	Thr	Arg
			30	
Thr	Met	His	Trp	Val
		35		
Arg	Gln	Ala	Pro	Gly
		40		
Gln	Gly	Leu	Glu	Trp
		45		
Gly	Tyr	Ile	Asn	Pro
	50			
Ser	Arg	Gly	Tyr	Thr
	55			
Asn	Tyr	Ala	Asp	Ser
	60			
Lys	Gly	Arg	Phe	Thr
	65			
Ile	Thr	Thr	Asp	Lys
	70			
Ser	Thr	Ser	Thr	Ala
	75			
Tyr	Ala	Asp	Ser	Val
Met	Glu	Leu	Ser	Ser
			85	
Leu	Arg	Ser	Glu	Asp
			90	
Thr	Ala	Thr	Tyr	Tyr
				95
Cys				
Ala	Arg	Tyr	Tyr	Asp
			100	
Asp	Asp	His	Tyr	Cys
				105
Leu	Asp	Tyr	Trp	Gly
				110
Gln	Gly			
Thr	Thr	Val	Thr	Val
		115		
Ser	Ser	Gly	Glu	Gly
		120		
Thr	Ser	Thr	Gly	Ser
			125	
Gly	Ser	Gly	Gly	Ser
	130			
Gly	Gly	Ala	Asp	Asp
		135		
Ile	Val	Leu	Thr	Gln
	140			
Ser				
Pro	Ala	Thr	Leu	Ser
	145			
Ser	Leu	Ser	Pro	Gly
	150			
Glu	Arg	Ala	Thr	Leu
	155			
Ser	Cys			
	160			
Arg	Ala	Ser	Gln	Ser
			165	
Val	Ser	Tyr	Met	Asn
				170
Trp	Tyr	Gln	Gln	Lys
				175
Pro				
Gly	Lys	Ala	Pro	Lys
			180	
Arg	Trp	Ile	Tyr	Asp
			185	
Thr	Ser	Lys	Val	Ala
			190	
Ser				
Gly	Val	Pro	Ala	Arg
	195			
Phe	Ser	Gly	Ser	Gly
		200		
Thr	Asp	Tyr	Ser	
	205			
Leu	Thr	Ile	Asn	Ser
	210			
Leu	Glu	Ala	Glu	Asp
	215			
Ala	Ala	Thr	Tyr	Tyr
	220			
Cys				
Gln	Gln	Trp	Ser	Ser
	225			
Asn	Pro	Leu	Thr	Phe
	230			
Gly	Gly	Gly	Thr	Lys
	235			
Val				
Glu	Ile	Lys	Ser	Gly
			245	
Gly	Gly	Gly	Ser	Asp

Tyr Gln Gln Ile Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr Asp Ala
 290 295 300
 Ser Asn Leu Val Ser Gly Ile Pro Pro Arg Phe Ser Gly Ser Gly Ser
 305 310 315 320
 Gly Thr Asp Phe Thr Leu Asn Ile His Pro Val Glu Lys Val Asp Ala
 325 330 335
 Ala Thr Tyr His Cys Gln Gln Ser Thr Glu Asp Pro Trp Thr Phe Gly
 340 345 350
 Gly Gly Thr Lys Leu Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly Gly
 355 360 365
 Gly Ser Gly Gly Gly Gly Ser Gln Val Gln Leu Gln Gln Ser Gly Ala
 370 375 380
 Glu Leu Val Arg Pro Gly Ser Ser Val Lys Ile Ser Cys Lys Ala Ser
 385 390 395 400
 Gly Tyr Ala Phe Ser Ser Tyr Trp Met Asn Trp Val Lys Gln Arg Pro
 405 410 415
 Gly Gln Gly Leu Glu Trp Ile Gly Gln Ile Trp Pro Gly Asp Gly Asp
 420 425 430
 Thr Asn Tyr Asn Gly Lys Phe Lys Gly Lys Ala Thr Leu Thr Ala Asp
 435 440 445
 Glu Ser Ser Ser Thr Ala Tyr Met Gln Leu Ser Ser Leu Ala Ser Glu
 450 455 460
 Asp Ser Ala Val Tyr Phe Cys Ala Arg Arg Glu Thr Thr Thr Val Gly
 465 470 475 480
 Arg Tyr Tyr Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr
 485 490 495
 Val Ser Ser

<210> 342

<211> 1494

<212> DNA

<213> artificial sequence

<220>

<223> VL3VH5xCD19 LHHL

<400> 342
 gacattgtac tgacccagtc tccagcaact ctgtctctgt ctccagggga gcgtgccacc 60
 ctgacctgca gagccagttc aagtgttaagt tacatgaact ggtaccagca gaagccgggc 120
 aaggcaccca aaagatggat ttatgacaca tccaaagtgg cttctggagt ccctgctcgc 180
 ttcagtggca gtgggtctgg gaccgactac tctctcaca tcaacagctt ggaggctgaa 240
 gatgctgcca cttattactg ccaacagtgg agtagtaacc cgctcacgtt cgggtggcggg 300
 accaaggtgg agatcaaagg cgaagggtact agtactgggt ctggtggaag tggagggttca 360
 ggtggagcag acgacgtcca actggtgcag tcaggggctg aagtgaaaaa acctggggcc 420
 tcagtgaagg tgtcctgcaa ggcttctggc tacaccttta ctaggtacac gatgcactgg 480
 gtaaggcagg cacctggaca gggctctggaa tggattggat acattaatcc tagccgtggg 540
 tatactaatt acgcagacag cgtcaagggc cgcttcacaa tcactacaga caaatccacc 600
 agcacagcct acatggaact gagcagcctg cgttctgagg aactgcaac ctattactgt 660
 gcaagatatt atgatgatca ttactgcctt gactactggg gccaaggcac cacggtcacc 720
 gtctcctccg gaggtgggtg atcccagggt cagctgcagc agtctggggc tgagctgggt 780
 aggcctgggt cctcagtga gatttcctgc aaggcttctg gctatgcatt cagtagctac 840
 tggatgaact ggggtgaagca gaggcctgga cagggtcttg agtggattgg acagatttgg 900
 cctggagatg gtgatactaa ctacaatgga aagttcaagg gtaaagccac tctgactgca 960
 gacgaatcct ccagcacagc ctacatgcaa ctcagcagcc tagcatctga ggactctgcg 1020
 gtctatttct gtgcaagacg ggagactacg acggtaggcc gttattacta tgctatggac 1080
 tactggggcc aagggaccac ggtcaccgtc tcctccgggt gtggtgggtc tggcggcggc 1140
 ggctccgggt gtggtgggtc tgatatccag ctgacccagt ctccagcttc tttggctgtg 1200
 tctctagggc agagggccac catctcctgc aaggccagcc aaagtgttga ttatgatggt 1260
 gatagttatt tgaactggta ccaacagatt ccaggacagc cacccaaact cctcatctat 1320
 gatgcatcca atctagtttc tgggatccca cccaggttta gtggcagtgg gtctgggaca 1380
 gacttcaccc tcaacatcca tcctgtggag aagggtggat ctgcaaccta tcaactgtcag 1440
 caaagtactg aggatccgtg gacgttcggt ggaggggacca agctcgagat caaa 1494

<210> 343

<211> 498

<212> PRT

<213> artificial sequence

<220>

<223> VL3VH5xCD19 LHHL

<400> 343

Asp Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
1 5 10 15

Glu Arg Ala Thr Leu Thr Cys Arg Ala Ser Ser Ser Val Ser Tyr Met
20 25 30

Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr
35 40 45

Asp Thr Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
50 55 60

Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu
65 70 75 80

Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr
85 90 95

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Gly Glu Gly Thr Ser Thr
100 105 110

Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Val Gln Leu
115 120 125

Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val
130 135 140

Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp
145 150 155 160

Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn
165 170 175

Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val Lys Gly Arg Phe
180 185 190

Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser
195 200 205

Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys Ala Arg Tyr Tyr
210 215 220

Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr
225 230 235 240

Val Ser Ser Gly Gly Gly Gly Ser Gln Val Gln Leu Gln Gln Ser Gly
245 250 255

Ala Glu Leu Val Arg Pro Gly Ser Ser Val Lys Ile Ser Cys Lys Ala
260 265 270

Ser Gly Tyr Ala Phe Ser Ser Tyr Trp Met Asn Trp Val Lys Gln Arg
 275 280 285

Pro Gly Gln Gly Leu Glu Trp Ile Gly Gln Ile Trp Pro Gly Asp Gly
 290 295 300

Asp Thr Asn Tyr Asn Gly Lys Phe Lys Gly Lys Ala Thr Leu Thr Ala
 305 310 315 320

Asp Glu Ser Ser Ser Thr Ala Tyr Met Gln Leu Ser Ser Leu Ala Ser
 325 330 335

Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg Arg Glu Thr Thr Thr Val
 340 345 350

Gly Arg Tyr Tyr Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Thr Val
 355 360 365

Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
 370 375 380

Gly Gly Ser Asp Ile Gln Leu Thr Gln Ser Pro Ala Ser Leu Ala Val
 385 390 395 400

Ser Leu Gly Gln Arg Ala Thr Ile Ser Cys Lys Ala Ser Gln Ser Val
 405 410 415

Asp Tyr Asp Gly Asp Ser Tyr Leu Asn Trp Tyr Gln Gln Ile Pro Gly
 420 425 430

Gln Pro Pro Lys Leu Leu Ile Tyr Asp Ala Ser Asn Leu Val Ser Gly
 435 440 445

Ile Pro Pro Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu
 450 455 460

Asn Ile His Pro Val Glu Lys Val Asp Ala Ala Thr Tyr His Cys Gln
 465 470 475 480

~~Gln Ser Thr Glu Asp Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu Glu~~
 485 490 495

Ile Lys

<210> 344

<211> 1497

<212> DNA

<213> artificial sequence

<220>

<223> VH5VL3xCD19 HLHL

<400> 344

gacgtccaac	tggtgcagtc	aggggctgaa	gtgaaaaaac	ctggggcctc	agtgaagggtg	60
tcctgcaagg	cttctggcta	cacctttact	aggtacacga	tgcactgggt	aaggcaggca	120
cctggacagg	gtctggaatg	gattggatac	attaatccta	gccgtgggta	tactaattac	180
gcagacagcg	tcaagggccg	cttcacaatc	actacagaca	aatccaccag	cacagcctac	240
atggaactga	gcagcctgcg	ttctgaggac	actgcaacct	attactgtgc	aagatattat	300
gatgatcatt	actgccttga	ctactggggc	caaggcacca	cggtcaccgt	ctcctcaggc	360
gaagg tacta	gtactggttc	tggtggaagt	ggagggttcag	gtggagcaga	cgacattgta	420
ctgacccagt	ctccagcaac	tctgtctctg	tctccagggg	agcgtgccac	cctgacctgc	480
agagccagtt	caagtgtaag	ttacatgaac	tggtaccagc	agaagccggg	caaggcaccc	540
aaaagatgga	tttatgacac	atccaaagtg	gcttctggag	tccctgctcg	cttcagtggc	600
agtgggtctg	ggaccgacta	ctctctcaca	atcaacagct	tggaggctga	agatgctgcc	660
acttattact	gccaacagtg	gagtagtaac	ccgctcacgt	tcggtggcgg	gaccaagggtg	720
gagatcaa at	ccggagggtg	tggatcccag	gtgcagctgc	agcagtctgg	ggctgagctg	780
gtgaggcctg	ggtcctcagt	gaagatttcc	tgcaaggctt	ctggctatgc	attcagtagc	840
tactggatga	actgggtgaa	gcagaggcct	ggacagggtc	ttgagtggat	tggacagatt	900
tggcctggag	atggtgatac	taactacaat	ggaaagttca	agggtaaagc	cactctgact	960
gcagacgaat	cctccagcac	agcctacatg	caactcagca	gcctagcatc	tgaggactct	1020
gcggtctatt	tctgtgcaag	acgggagact	acgacggtag	gccgttatta	ctatgctatg	1080
gactactggg	gccaagggac	cacggtcacc	gtctcctccg	gtgggtgggtg	ttctggcggc	1140
ggcggctccg	gtgggtgggtg	ttctgatatc	cagctgaccc	agtctccagc	ttctttggct	1200
gtgtctctag	ggcagagggc	caccatctcc	tgcaaggcca	gccaaagtgt	tgattatgat	1260
ggtgatagtt	atttgaactg	gtaccaacag	attccaggac	agccacccaa	actcctcatc	1320
tatgatgcat	ccaatctagt	ttctgggatc	ccacccagggt	ttagtggcag	tgggtctggg	1380
acagacttca	ccctcaacat	ccatcctgtg	gagaagggtg	atgctgcaac	ctatcactgt	1440
cagcaaagta	ctgaggatcc	gtggacgttc	ggtggaggga	ccaagctcga	gatcaaaa	1497

<210> 345

<211> 499

<212> PRT

<213> artificial sequence

<220>

<223> VH5VL3xCD19 HLHL

<400> 345

Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
 1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr
 20 25 30

Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
 35 40 45

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val
 50 55 60

Lys Gly Arg Phe Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr
 65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys
 85 90 95

Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
 100 105 110

Thr Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly
 115 120 125

Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Val Leu Thr Gln Ser
 130 135 140

Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Thr Cys
 145 150 155 160

Arg Ala Ser Ser Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro
 165 170 175

Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser
 180 185 190

Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser
 195 200 205

Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys
 210 215 220

Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
 225 230 235 240

Glu Ile Lys Ser Gly Gly Gly Gly Ser Gln Val Gln Leu Gln Gln Ser
 245 250 255

Gly Ala Glu Leu Val Arg Pro Gly Ser³⁵⁵ Ser Val Lys Ile Ser Cys Lys
 260 265 270
 Ala Ser Gly Tyr Ala Phe Ser Ser Tyr Trp Met Asn Trp Val Lys Gln
 275 280 285
 Arg Pro Gly Gln Gly Leu Glu Trp Ile Gly Gln Ile Trp Pro Gly Asp
 290 295 300
 Gly Asp Thr Asn Tyr Asn Gly Lys Phe Lys Gly Lys Ala Thr Leu Thr
 305 310 315 320
 Ala Asp Glu Ser Ser Ser Thr Ala Tyr Met Gln Leu Ser Ser Leu Ala
 325 330 335
 Ser Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg Arg Glu Thr Thr Thr
 340 345 350
 Val Gly Arg Tyr Tyr Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Thr
 355 360 365
 Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
 370 375 380
 Gly Gly Gly Ser Asp Ile Gln Leu Thr Gln Ser Pro Ala Ser Leu Ala
 385 390 395 400
 Val Ser Leu Gly Gln Arg Ala Thr Ile Ser Cys Lys Ala Ser Gln Ser
 405 410 415
 Val Asp Tyr Asp Gly Asp Ser Tyr Leu Asn Trp Tyr Gln Gln Ile Pro
 420 425 430
 Gly Gln Pro Pro Lys Leu Leu Ile Tyr Asp Ala Ser Asn Leu Val Ser
 435 440 445
 Gly Ile Pro Pro Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr
 450 455 460
 Leu Asn Ile His Pro Val Glu Lys Val Asp Ala Ala Thr Tyr His Cys
 465 470 475 480
 Gln Gln Ser Thr Glu Asp Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu
 485 490 495
 Glu Ile Lys

<210> 346

<211> 1494

<212> DNA

<213> artificial sequence

<220>

<223> VL3VH5xCD19 LHLH

<400> 346
gacattgtac tgacccagtc tccagcaact ctgtctctgt ctccagggga gcgtgccacc 60
ctgacctgca gagccagttc aagtgttaagt tacatgaact ggtaccagca gaagccgggc 120
aaggcaccca aaagatggat ttatgacaca tccaaagtgg cttctggagt ccctgctcgc 180
ttcagtggca gtgggtctgg gaccgactac tctctcacia tcaacagctt ggaggctgaa 240
gatgctgcca cttattactg ccaacagtgg agtagtaacc cgctcacgtt cgggtggcggg 300
accaaggtgg agatcaaagg cgaaggtact agtactgggt ctggtggaag tggaggttca 360
ggtggagcag acgacgtcca actggtgcag tcaggggctg aagtgaaaaa acctggggcc 420
tcagtgaagg tgtcctgcaa ggcttctggc tacaccttta ctaggtacac gatgcactgg 480
gtaaggcagg cacctggaca gggctctggaa tggattggat acattaatcc tagccgtggt 540
tatactaatt acgcagacag cgtcaagggc cgcttcacaa tctactacaga caaatccacc 600
agcacagcct acatggaact gagcagcctg cgcttctgagg aactgcaac ctattactgt 660
gcaagatatt atgatgatca ttactgcctt gactactggg gccaaaggcac cacggtcacc 720
gtctcctccg gaggtgggtgg atccgatatc cagctgaccc agtctccagc ttctttggct 780
gtgtctctag ggcagagggc caccatctcc tgcaaggcca gccaaagtgt tgattatgat 840
ggtgatagtt atttgaactg gtaccaacag attccaggac agccacccaa actcctcatc 900
tatgatgcat ccaatctagt ttctgggatc ccaccaggt ttagtggcag tgggtctggg 960
acagacttca ccctcaacat ccctcctgtg gagaaggtgg atgctgcaac ctatcactgt 1020
cagcaaagta ctgaggatcc gtggacgttc ggtggaggga ccaagctcga gatcaaaggt 1080
ggtggtgggt ctggcggcgg cggtcccggt ggtggtgggt ctcaggtgca gctgcagcag 1140
tctggggctg agctggtgag gcctgggtcc tcagtgaaga tttcctgcaa ggcttctggc 1200
tatgcattca gtagctactg gatgaactgg gtgaagcaga ggcctggaca gggctctgag 1260
tggattggac agatttggcc tggagatggt gatactaact acaatggaaa gttcaagggt 1320
aaagccactc tgactgcaga cgaatcctcc agcacagcct acatgcaact cagcagccta 1380
gcatctgagg actctgcggt ctatttctgt gcaagacggg agactacgac ggtaggccgt 1440
tattactatg ctatggacta ctggggccaa gggaccacgg tcaccgtctc ctcc 1494

<210> 347

<211> 498

<212> PRT

<213> artificial sequence

<220>

<223> VL3VH5xCD19 LHLH

<400> 347

Asp Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
1 5 10 15

Glu Arg Ala Thr Leu Thr Cys Arg Ala Ser Ser Ser Val Ser Tyr Met
20 25 30

Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr
35 40 45

Asp Thr Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
50 55 60

Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu
65 70 75 80

Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr
85 90 95

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Gly Glu Gly Thr Ser Thr
100 105 110

Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Val Gln Leu
115 120 125

Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val
130 135 140

Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp
145 150 155 160

Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn
165 170 175

Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val Lys Gly Arg Phe
180 185 190

Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser
195 200 205

Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys Ala Arg Tyr Tyr
210 215 220

Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr
225 230 235 240

Val Ser Ser Gly Gly Gly Gly Ser Asp Ile Gln Leu Thr Gln Ser Pro

245 358 255
 250
 Ala Ser Leu Ala Val Ser Leu Gly Gln Arg Ala Thr Ile Ser Cys Lys
 260 265 270
 Ala Ser Gln Ser Val Asp Tyr Asp Gly Asp Ser Tyr Leu Asn Trp Tyr
 275 280 285
 Gln Gln Ile Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr Asp Ala Ser
 290 295 300
 Asn Leu Val Ser Gly Ile Pro Pro Arg Phe Ser Gly Ser Gly Ser Gly
 305 310 315 320
 Thr Asp Phe Thr Leu Asn Ile His Pro Val Glu Lys Val Asp Ala Ala
 325 330 335
 Thr Tyr His Cys Gln Gln Ser Thr Glu Asp Pro Trp Thr Phe Gly Gly
 340 345 350
 Gly Thr Lys Leu Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly
 355 360 365
 Ser Gly Gly Gly Gly Ser Gln Val Gln Leu Gln Gln Ser Gly Ala Glu
 370 375 380
 Leu Val Arg Pro Gly Ser Ser Val Lys Ile Ser Cys Lys Ala Ser Gly
 385 390 395 400
 Tyr Ala Phe Ser Ser Tyr Trp Met Asn Trp Val Lys Gln Arg Pro Gly
 405 410 415
 Gln Gly Leu Glu Trp Ile Gly Gln Ile Trp Pro Gly Asp Gly Asp Thr
 420 425 430
 Asn Tyr Asn Gly Lys Phe Lys Gly Lys Ala Thr Leu Thr Ala Asp Glu
 435 440 445
 Ser Ser Ser Thr Ala Tyr Met Gln Leu Ser Ser Leu Ala Ser Glu Asp
 450 455 460
 Ser Ala Val Tyr Phe Cys Ala Arg Arg Glu Thr Thr Thr Val Gly Arg
 465 470 475 480
 Tyr Tyr Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val
 485 490 495
 Ser Ser

<211> 1497

<212> DNA

<213> artificial sequence

<220>

<223> VH5VL3xCD19 HLLH

<400> 348

gacgtccaac tggcgcagtc aggggctgaa gtgaaaaaac ctggggcctc agtgaagggtg	60
tcctgcaagg cttctggcta cacctttact aggtacacga tgcactgggt aaggcaggca	120
cctggacagg gtctggaatg gattggatac attaatccta gccgtgggtta tactaattac	180
gcagacagcg tcaagggccg cttcacaatc actacagaca aatccaccag cacagcctac	240
atggaactga gcagcctgcg ttctgaggac actgcaacct attactgtgc aagatattat	300
gatgatcatt actgccttga ctactggggc caaggcacca cggtcaccgt ctcctcaggc	360
gaaggtacta gtactgggtc tggcgggaagt ggaggttcag gtggagcaga cgacattgta	420
ctgacccagt ctccagcaac tctgtctctg tctccagggg agcgtgccac cctgacctgc	480
agagccagtt caagtgtgaa ttacatgaac tggcaccagc agaagccggg caaggcaccc	540
aaaagatgga tttatgacac atccaaagtg gcttctggag tccctgctcg cttcagtggc	600
agtgggtctg ggaccgacta ctctctcaca atcaacagct tggaggctga agatgctgcc	660
acttattact gccaacagtg gagtagtaac ccgctcacgt tcggcggcgg gaccaagggtg	720
gagatcaaat ccggagggtg tggatccgat atccagctga cccagtctcc agcttctttg	780
gctgtgtctc tagggcagag ggccaccatc tcctgcaagg ccagccaaag tgttgattat	840
gatggtgata gttatttgaa ctggtaccaa cagattccag gacagccacc caaactcctc	900
atctatgatg catccaatct agtttctggg atcccaccca ggtttagtgg cagtgggtct	960
gggacagact tcaccctcaa catccatcct gtggagaagg tggatgctgc aacctatcac	1020
tgtcagcaaa gtactgagga tccgtggacg ttcggcggag ggaccaagct cgagatcaaa	1080
ggcggcgggtg gttctggcgg cggcggctcc ggcggcgggtg gttctcagggt gcagctgcag	1140
cagtctgggg ctgagctggt gaggcctggg tcctcagtga agatttcctg caaggcttct	1200
ggctatgcat tcagtagcta ctggatgaac tgggtgaagc agaggcctgg acagggtctt	1260
gagtggattg gacagatttg gcctggagat ggtgatacta actacaatgg aaagttcaag	1320
ggtaaagcca ctctgactgc agacgaatcc tccagcacag cctacatgca actcagcagc	1380
ctagcatctg aggactctgc ggtctatttc tgtgcaagac gggagactac gacggtaggc	1440
cgttattact atgctatgga ctactggggc caagggacca cggtcaccgt ctcctcc	1497

<210> 349

<211> 499

<212> PRT

<213> artificial sequence

<220>

<223> VH5VL3xCD19 HLLH

<400> 349

Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr
20 25 30

Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys
85 90 95

Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly
115 120 125

Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Val Leu Thr Gln Ser
130 135 140

Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Thr Cys
145 150 155 160

Arg Ala Ser Ser Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro
165 170 175

Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser
180 185 190

Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser
195 200 205

Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys
210 215 220

Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
225 230 235 240

Glu Ile Lys Ser Gly Gly Gly Gly Ser Asp Ile Gln Leu Thr Gln Ser
 245 250 255
 Pro Ala Ser Leu Ala Val Ser Leu Gly Gln Arg Ala Thr Ile Ser Cys
 260 265 270
 Lys Ala Ser Gln Ser Val Asp Tyr Asp Gly Asp Ser Tyr Leu Asn Trp
 275 280 285
 Tyr Gln Gln Ile Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr Asp Ala
 290 295 300
 Ser Asn Leu Val Ser Gly Ile Pro Pro Arg Phe Ser Gly Ser Gly Ser
 305 310 315 320
 Gly Thr Asp Phe Thr Leu Asn Ile His Pro Val Glu Lys Val Asp Ala
 325 330 335
 Ala Thr Tyr His Cys Gln Gln Ser Thr Glu Asp Pro Trp Thr Phe Gly
 340 345 350
 Gly Gly Thr Lys Leu Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly Gly
 355 360 365
 Gly Ser Gly Gly Gly Gly Ser Gln Val Gln Leu Gln Gln Ser Gly Ala
 370 375 380
 Glu Leu Val Arg Pro Gly Ser Ser Val Lys Ile Ser Cys Lys Ala Ser
 385 390 395 400
 Gly Tyr Ala Phe Ser Ser Tyr Trp Met Asn Trp Val Lys Gln Arg Pro
 405 410 415
 Gly Gln Gly Leu Glu Trp Ile Gly Gln Ile Trp Pro Gly Asp Gly Asp
 420 425 430
 Thr Asn Tyr Asn Gly Lys Phe Lys Gly Lys Ala Thr Leu Thr Ala Asp
 435 440 445
 Glu Ser Ser Ser Thr Ala Tyr Met Gln Leu Ser Ser Leu Ala Ser Glu
 450 455 460
 Asp Ser Ala Val Tyr Phe Cys Ala Arg Arg Glu Thr Thr Thr Val Gly
 465 470 475 480
 Arg Tyr Tyr Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr
 485 490 495

Val Ser Ser

<210> 350
 <211> 1494
 <212> DNA
 <213> artificial sequence

<220>

<223> VL1VH7xCD19 LHHL

<400> 350
 gacattcaga tgacccagtc tccatctagc ctgtctgcat ctgtcgggga ccgtgtcacc 60
 atcacctgca gagccagtca aagtgttaagt tacatgaact ggtaccagca gaagccgggc 120
 aaggcaccga aaagatggat ttatgacaca tccaaagtgg cttctggagt ccctgctcgc 180
 ttcagtggca gtgggtctgg gaccgactac tctctcacia tcaacagctt ggaggctgaa 240
 gatgctgcca cttattactg ccaacagtgg agtagtaacc cgctcacgtt cggtggcggg 300
 accaaggtgg agatcaaagg cgaaggtact agtactgggt ctggtggaag tggagggttca 360
 ggtggagcag acgacgtcca actggtgcag tcaggggctg aagtgaaaaa acctggggcc 420
 tcagtgaagg tgtcctgcaa ggcttctggc tacaccttta ctaggtacac gatgcactgg 480
 gtaaggcagg cacctggaca gggctctggaa tggattggat acattaatcc tagccgtggg 540
 tatactaatt acaatcagaa gttcaaggac cgcgtcacia tcactacaga caaatccacc 600
 agcacagcct acatggaact gagcagcctg cgttctgagg aactgacagt ctattactgt 660
 gcaagatatt atgatgatca ttactgcctt gactactggg gccaaaggcac cacggtcacc 720
 gtctcctccg gaggtgggtg atcccagggtg cagctgcagc agtctggggc tgagctgggtg 780
 aggcctgggt cctcagtga gatttcctgc aaggcttctg gctatgcatt cagtagctac 840
 tggatgaact ggggtgaagca gaggcctgga cagggtcttg agtggattgg acagatttgg 900
 cctggagatg gtgatactaa ctacaatgga aagttcaagg gtaaagccac tctgactgca 960
 gacgaatcct ccagcacagc ctacatgcaa ctcagcagcc tagcatctga ggactctgcg 1020
 gtctatttct gtgcaagacg ggagactacg acggtaggcc gttattacta tgctatggac 1080
 tactggggcc aagggaccac ggtcaccgtc tcctccgggtg gtggtgggtc tggcggcggc 1140
 ggctccgggtg gtggtgggtc tgatatccag ctgacccagt ctccagcttc tttggctgtg 1200
 tctctagggc agagggccac catctcctgc aaggccagcc aaagtgttga ttatgatggg 1260
 gatagttatt tgaactggta ccaacagatt ccaggacagc caccctaaact cctcatctat 1320
 gatgcatcca atctagtttc tgggatccca cccagggttta gtggcagtgg gtctggggaca 1380
 gacttcaccc tcaacatcca tcctgtggag aagggtggatg ctgcaaccta tcaactgtcag 1440
 caaagtactg aggatccgtg gacgttcggg ggagggacca agctcgagat caaa 1494

<210> 351

<211> 498

<212> PRT

<213> artificial sequence

<220>

<223> VL1VH7xCD19 LHHL

<400> 351

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Ser Tyr Met
20 25 30

Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr
35 40 45

Asp Thr Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
50 55 60

Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu
65 70 75 80

Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr
85 90 95

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Gly Glu Gly Thr Ser Thr
100 105 110

Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Val Gln Leu
115 120 125

Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val
130 135 140

Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp
145 150 155 160

Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn
165 170 175

Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe Lys Asp Arg Val
180 185 190

Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser
195 200 205

Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Tyr Tyr
210 215 220

Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr
225 230 235 240

Val Ser Ser Gly Gly Gly Gly Ser Gln Val Gln Leu Gln Gln Ser Gly
245 250 255

Ala Glu Leu Val Arg Pro Gly Ser Ser Val Lys Ile Ser Cys Lys Ala
260 265 270

Ser Gly Tyr Ala Phe Ser Ser Tyr Trp Met Asn Trp Val Lys Gln Arg
275 280 285

Pro Gly Gln Gly Leu Glu Trp Ile Gly Gln Ile Trp Pro Gly Asp Gly
290 295 300

Asp Thr Asn Tyr Asn Gly Lys Phe Lys Gly Lys Ala Thr Leu Thr Ala
305 310 315 320

Asp Glu Ser Ser Ser Thr Ala Tyr Met Gln Leu Ser Ser Leu Ala Ser
325 330 335

Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg Arg Glu Thr Thr Thr Val
340 345 350

Gly Arg Tyr Tyr Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Thr Val
355 360 365

Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
370 375 380

Gly Gly Ser Asp Ile Gln Leu Thr Gln Ser Pro Ala Ser Leu Ala Val
385 390 395 400

Ser Leu Gly Gln Arg Ala Thr Ile Ser Cys Lys Ala Ser Gln Ser Val
405 410 415

Asp Tyr Asp Gly Asp Ser Tyr Leu Asn Trp Tyr Gln Gln Ile Pro Gly
420 425 430

Gln Pro Pro Lys Leu Leu Ile Tyr Asp Ala Ser Asn Leu Val Ser Gly
435 440 445

Ile Pro Pro Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu
450 455 460

Asn Ile His Pro Val Glu Lys Val Asp Ala Ala Thr Tyr His Cys Gln
465 470 475 480

Gln Ser Thr Glu Asp Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu Glu
485 490 495

Ile Lys

<210> 352

<211> 1497

<212> DNA

<213> artificial sequence

<220>

<223> VH7VL1xCD19 HLHL

<400> 352

gacgtccaac	tggtgcagtc	aggggctgaa	gtgaaaaaac	ctggggcctc	agtgaaggtg	60
tcctgcaagg	cttctggcta	cacctttact	aggtacacga	tgactgggt	aaggcaggca	120
cctggacagg	gtctggaatg	gattggatac	attaatccta	gccgtgggta	tactaattac	180
aatcagaagt	tcaaggaccg	cgtcacaatc	actacagaca	aatccaccag	cacagcctac	240
atggaactga	gcagcctgcg	ttctgaggac	actgcagtct	attactgtgc	aagatattat	300
gatgatcatt	actgccttga	ctactggggc	caaggcacca	cggtcaccgt	ctcctcaggc	360
gaaggtacta	gtactgggtc	tggtggaagt	ggagggttcag	gtggagcaga	cgacattcag	420
atgacccagt	ctccatctag	cctgtctgca	tctgtcgggg	accgtgtcac	catcacctgc	480
agagccagtc	aaagtgtaag	ttacatgaac	tggtaccagc	agaagccggg	caaggcaccc	540
aaaagatgga	tttatgacac	atccaaagtg	gcttctggag	tccctgctcg	cttcagtggc	600
agtgggtctg	ggaccgacta	ctctctcaca	atcaacagct	tggaggctga	agatgctgcc	660
acttattact	gccaacagtg	gagtagtaac	ccgctcacgt	tcgggtggcg	gaccaaggtg	720
gagatcaa	at ccggaggtgg	tggatcccag	gtgcagctgc	agcagtctgg	ggctgagctg	780
gtgaggcctg	ggtcctcagt	gaagatttcc	tgcaaggctt	ctggctatgc	attcagtagc	840
tactggatga	actgggtgaa	gcagaggcct	ggacagggtc	ttgagtggat	tggacagatt	900
tggcctggag	atgggtgatac	taactacaat	ggaaagttca	agggtaaagc	cactctgact	960
gcagacgaat	cctccagcac	agcctacatg	caactcagca	gcctagcatc	tgaggactct	1020
gcgggtctatt	tctgtgcaag	acgggagact	acgacggtag	gccgttatta	ctatgctatg	1080
gactactggg	gccaagggac	cacggtcacc	gtctcctccg	gtgggtgggtg	ttctggcggc	1140
ggcggctccg	gtgggtgggtg	ttctgatatc	cagctgaccc	agtctccagc	ttctttggct	1200
gtgtctctag	ggcagagggc	caccatctcc	tgcaaggcca	gccaaagtgt	tgattatgat	1260
ggatgatagtt	atttgaactg	gtaccaacag	attccaggac	agccacccaa	actcctcatc	1320
tatgatgcat	ccaatctagt	ttctgggatc	ccaccaggt	ttagtggcag	tgggtctggg	1380
acagacttca	ccctcaacat	ccatcctgtg	gagaaggtgg	atgctgcaac	ctatcactgt	1440
cagcaaagta	ctgaggatcc	gtggacgttc	ggaggaggga	ccaagctcga	gatcaaa	1497

<210> 353
 <211> 499
 <212> PRT
 <213> artificial sequence

<220>

<223> VH7VL1xCD19 HLHL

<400> 353

Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
 1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr
 20 25 30

Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
 35 40 45

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe
 50 55 60

Lys Asp Arg Val Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr
 65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
 85 90 95

Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
 100 105 110

Thr Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly
 115 120 125

Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Gln Met Thr Gln Ser
 130 135 140

Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys
 145 150 155 160

Arg Ala Ser Gln Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro
 165 170 175

Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser
 180 185 190

Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser
 195 200 205

Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala³⁶⁷ Ala Thr Tyr Tyr Cys
 210 215 220

Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
 225 230 235 240

Glu Ile Lys Ser Gly Gly Gly Gly Ser Gln Val Gln Leu Gln Gln Ser
 245 250 255

Gly Ala Glu Leu Val Arg Pro Gly Ser Ser Val Lys Ile Ser Cys Lys
 260 265 270

Ala Ser Gly Tyr Ala Phe Ser Ser Tyr Trp Met Asn Trp Val Lys Gln
 275 280 285

Arg Pro Gly Gln Gly Leu Glu Trp Ile Gly Gln Ile Trp Pro Gly Asp
 290 295 300

Gly Asp Thr Asn Tyr Asn Gly Lys Phe Lys Gly Lys Ala Thr Leu Thr
 305 310 315 320

Ala Asp Glu Ser Ser Ser Thr Ala Tyr Met Gln Leu Ser Ser Leu Ala
 325 330 335

Ser Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg Arg Glu Thr Thr Thr
 340 345 350

Val Gly Arg Tyr Tyr Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Thr
 355 360 365

Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
 370 375 380

Gly Gly Gly Ser Asp Ile Gln Leu Thr Gln Ser Pro Ala Ser Leu Ala
 385 390 395 400

Val Ser Leu Gly Gln Arg Ala Thr Ile Ser Cys Lys Ala Ser Gln Ser
 405 410 415

Val Asp Tyr Asp Gly Asp Ser Tyr Leu Asn Trp Tyr Gln Gln Ile Pro
 420 425 430

Gly Gln Pro Pro Lys Leu Leu Ile Tyr Asp Ala Ser Asn Leu Val Ser
 435 440 445

Gly Ile Pro Pro Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr
 450 455 460

Leu Asn Ile His Pro Val Glu Lys Val Asp Ala Ala Thr Tyr His Cys
 465 470 475 480

Gln Gln Ser Thr Glu Asp Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu

Glu Ile Lys

<210> 354

<211> 1494

<212> DNA

<213> artificial sequence

<220>

<223> VL1VH7xCD19 LHLH

<400> 354

gacattcaga tgacccagtc tccatctagc ctgtctgcat ctgtcgggga ccgtgtcacc	60
atcacctgca gagccagtca aagtgtaagt tacatgaact ggtaccagca gaagccgggc	120
aaggcaccca aaagatggat ttatgacaca tccaaagtgg cttctggagt ccctgctcgc	180
ttcagtggca gtgggtctgg gaccgactac tctctcacia tcaacagctt ggaggctgaa	240
gatgctgcca cttattactg ccaacagtgg agtagtaacc cgctcacgtt cggtggcggg	300
accaaggtgg agatcaaagg cgaagggtact agtactgggt ctggtggaag tggagggttca	360
ggtggagcag acgacgtcca actgggtgcag tcaggggctg aagtgaaaaa acctggggcc	420
tcagtgaagg tgtcctgcaa ggcttctggc tacaccttta ctaggtacac gatgcactgg	480
gtaaggcagg cacctggaca gggctctggaa tggattggat acattaatcc tagccgtggt	540
tatactaatt acaatcagaa gttcaaggac cgcgtcacia tcactacaga caaatccacc	600
agcacagcct acatggaact gagcagcctg cgcttctgagg aactgacagt ctattactgt	660
gcaagatatt atgatgatca ttactgcctt gactactggg gccaaggcac cacggtcacc	720
gtctcctccg gaggtgggtgg atccgatatc cagctgaccc agtctccagc ttctttggct	780
gtgtctctag ggcagagggc caccatctcc tgcaaggcca gccaaagtgt tgattatgat	840
ggtgatagtt atttgaactg gtaccaacag attccaggac agccacccaa actcctcatc	900
tatgatgcat ccaatctagt ttctgggatc ccacccagggt ttagtggcag tgggtctggg	960
acagacttca ccctcaacat ccctcctgtg gagaagggtg atgctgcaac ctatcactgt	1020
cagcaaagta ctgaggatcc gtggacgttc ggtggaggga ccaagctcga gatcaaagg	1080
ggtgggtggt ctggcggcgg cggctccggt ggtgggtggt ctcagggtgca gctgcagcag	1140
tctggggctg agctgggtgag gcctgggtcc tcagtgaaga tttcctgcaa ggcttctggc	1200
tatgcattca gtagctactg gatgaactgg gtgaagcaga ggcctggaca gggctcttgag	1260
tggattggac agatttggcc tggagatggg gatactaact acaatggaaa gttcaagggt	1320
aaagccactc tgactgcaga cgaatcctcc agcacagcct acatgcaact cagcagccta	1380
gcatctgagg actctgcggt ctatttctgt gcaagacggg agactacgac ggtaggccgt	1440

tattactatg ctatggacta ctggggccaa gggaccacgg tcaccgtctc ctcc

1494

<210> 355

<211> 498

<212> PRT

<213> artificial sequence

<220>

<223> VL1VH7xCD19 LHLH

<400> 355

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Ser Tyr Met
20 25 30

Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr
35 40 45

Asp Thr Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
50 55 60

Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu
65 70 75 80

Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr
85 90 95

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Gly Glu Gly Thr Ser Thr
100 105 110

Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Val Gln Leu
115 120 125

Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val
130 135 140

Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp
145 150 155 160

Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn
165 170 175

Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe Lys Asp Arg Val
180 185 190

Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser

195	200	370	205
Ser 210	Leu Arg Ser Glu Asp Thr 215	Ala Val Tyr Tyr Cys 220	Ala Arg Tyr Tyr
Asp 225	Asp His Tyr Cys 230	Leu Asp Tyr Trp Gly Gln 235	Gly Thr Thr Val Thr 240
Val Ser Ser Gly 245	Gly Gly Gly Ser Asp Ile 250	Gln Leu Thr Gln Ser 255	Pro
Ala Ser Leu 260	Ala Val Ser Leu Gly Gln 265	Arg Ala Thr Ile Ser 270	Cys Lys
Ala Ser Gln 275	Ser Val Asp Tyr Asp 280	Gly Asp Ser Tyr Leu 285	Asn Trp Tyr
Gln 290	Gln Ile Pro Gly Gln 295	Pro Pro Lys Leu Leu Ile 300	Tyr Asp Ala Ser
Asn 305	Leu Val Ser Gly Ile 310	Pro Pro Arg Phe Ser 315	Gly Ser Gly Ser Gly 320
Thr Asp Phe Thr 325	Leu Asn Ile His Pro Val 330	Glu Lys Val Asp Ala 335	Ala
Thr Tyr His Cys 340	Gln Gln Ser Thr Glu 345	Asp Pro Trp Thr Phe 350	Gly Gly
Gly Thr Lys 355	Leu Glu Ile Lys Gly 360	Gly Gly Gly Ser Gly 365	Gly Gly Gly
Ser Gly 370	Gly Gly Gly Ser Gln 375	Val Gln Leu Gln Gln 380	Ser Gly Ala Glu
Leu 385	Val Arg Pro Gly Ser 390	Ser Val Lys Ile Ser 395	Cys Lys Ala Ser Gly 400
Tyr Ala Phe Ser 405	Ser Tyr Trp Met Asn 410	Trp Val Lys Gln Arg Pro 415	Gly
Gln Gly Leu Glu 420	Trp Ile Gly Gln Ile 425	Trp Pro Gly Asp Gly 430	Asp Thr
Asn Tyr Asn 435	Gly Lys Phe Lys Gly 440	Lys Ala Thr Leu Thr 445	Ala Asp Glu
Ser 450	Ser Ser Thr Ala Tyr Met 455	Gln Leu Ser Ser Leu 460	Ala Ser Glu Asp
Ser 465	Ala Val Tyr Phe Cys 470	Ala Arg Arg Glu Thr 475	Thr Thr Val Gly Arg 480

Tyr Tyr Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val
485 490 495

Ser Ser

<210> 356

<211> 1497

<212> DNA

<213> artificial sequence

<220>

<223> VH7VL1xCD19 HLLH

<400> 356

gacgtccaac	tggtgcagtc	aggggctgaa	gtgaaaaaac	ctggggcctc	agtgaagggtg	60
tcctgcaagg	cttctggcta	cacctttact	aggtacacga	tgcactgggt	aaggcaggca	120
cctggacagg	gtctggaatg	gattggatac	attaatccta	gccgtggtta	tactaattac	180
aatcagaagt	tcaaggaccg	cgtcacaatc	actacagaca	aatccaccag	cacagcctac	240
atggaactga	gcagcctgcg	ttctgaggac	actgcagtct	attactgtgc	aagatattat	300
gatgatcatt	actgccttga	ctactggggc	caaggcacca	cggtcaccgt	ctcctcaggc	360
gaagg tacta	gtactggttc	tggtggaagt	ggagggttcag	gtggagcaga	cgacattcag	420
atgacc cagt	ctccatctag	cctgtctgca	tctgtcgggg	accgtgtcac	catcacctgc	480
agagccagtc	aaagtgt aag	ttacatgaac	tggtaccagc	agaagccggg	caaggcaccc	540
aaaagatgga	tttatgacac	atccaaagtg	gcttctggag	tccctgctcg	cttcagtggc	600
agtgggtctg	ggaccgacta	ctctctcaca	atcaacagct	tggaggctga	agatgctgcc	660
acttattact	gccaacagtg	gagtagtaac	ccgctcacgt	tcggtggcgg	gaccaagggtg	720
gagatcaaat	ccggagggtg	tggatccgat	atccagctga	cccagtctcc	agcttctttg	780
gctgtgtctc	tagggcagag	ggccaccatc	tcctgcaagg	ccagccaaag	tgttgattat	840
gatggtgata	gttattttgaa	ctggtaccaa	cagattccag	gacagccacc	caaactcctc	900
atctatgatg	catccaatct	agtttctggg	atcccaccca	ggttttagtg	cagtgggtct	960
gggacagact	tcaccctcaa	catccatcct	gtggagaagg	tggatgctgc	aacctatcac	1020
tgtcagcaaa	gtactgagga	tccgtggacg	ttcgggtggag	ggaccaagct	cgagatcaaa	1080
gggtggtggtg	gttctggcgg	cggcggctcc	ggtggtggtg	gttctcaggt	gcagctgcag	1140
cagtctgggg	ctgagctggt	gaggcctggg	tcctcagtga	agatttcctg	caaggcttct	1200
ggctatgcat	tcagtagcta	ctggatgaac	tgggtgaagc	agaggcctgg	acagggtctt	1260
gagtg gattg	gacagatttg	gcctggagat	ggtgatacta	actacaatgg	aaagttcaag	1320

372

ggtaaagcca ctctgactgc agacgaatcc tccagcacag cctacatgca actcagcagc	1380
ctagcatctg aggactctgc ggtctatttc tgtgcaagac gggagactac gacggtaggc	1440
cgttattact atgctatgga ctactggggc caagggacca cggtcaccgt ctctctcc	1497

<210> 357

<211> 499

<212> PRT

<213> artificial sequence

<220>

<223> VH7VL1XCD19 HLLH

<400> 357

Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr
20 25 30

Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe
50 55 60

Lys Asp Arg Val Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly
115 120 125

Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Gln Met Thr Gln Ser
130 135 140

Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys
145 150 155 160

Arg Ala Ser Gln Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro
165 170 175

Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser
180 185 190

Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser
 195 200 205
 Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys
 210 215 220
 Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
 225 230 235 240
 Glu Ile Lys Ser Gly Gly Gly Gly Ser Asp Ile Gln Leu Thr Gln Ser
 245 250 255
 Pro Ala Ser Leu Ala Val Ser Leu Gly Gln Arg Ala Thr Ile Ser Cys
 260 265 270
 Lys Ala Ser Gln Ser Val Asp Tyr Asp Gly Asp Ser Tyr Leu Asn Trp
 275 280 285
 Tyr Gln Gln Ile Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr Asp Ala
 290 295 300
 Ser Asn Leu Val Ser Gly Ile Pro Pro Arg Phe Ser Gly Ser Gly Ser
 305 310 315 320
 Gly Thr Asp Phe Thr Leu Asn Ile His Pro Val Glu Lys Val Asp Ala
 325 330 335
 Ala Thr Tyr His Cys Gln Gln Ser Thr Glu Asp Pro Trp Thr Phe Gly
 340 345 350
 Gly Gly Thr Lys Leu Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly Gly
 355 360 365
 Gly Ser Gly Gly Gly Gly Ser Gln Val Gln Leu Gln Gln Ser Gly Ala
 370 375 380
 Glu Leu Val Arg Pro Gly Ser Ser Val Lys Ile Ser Cys Lys Ala Ser
 385 390 395 400
 Gly Tyr Ala Phe Ser Ser Tyr Trp Met Asn Trp Val Lys Gln Arg Pro
 405 410 415
 Gly Gln Gly Leu Glu Trp Ile Gly Gln Ile Trp Pro Gly Asp Gly Asp
 420 425 430
 Thr Asn Tyr Asn Gly Lys Phe Lys Gly Lys Ala Thr Leu Thr Ala Asp
 435 440 445
 Glu Ser Ser Ser Thr Ala Tyr Met Gln Leu Ser Ser Leu Ala Ser Glu
 450 455 460

Asp Ser Ala Val Tyr Phe Cys Ala Arg Arg Glu Thr Thr Thr Val Gly
465 470 475 480

Arg Tyr Tyr Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr
485 490 495

Val Ser Ser

<210> 358

<211> 1494

<212> DNA

<213> artificial sequence

<220>

<223> VL2VH7xCD19 LHHL

<400> 358

gacattgtac	tgacccagtc	tccagcaact	ctgtctctgt	ctccagggga	gcgtgccacc	60
ctgagctgca	gagccagtca	aagtgttaagt	tacatgaact	ggtaccagca	gaagccgggc	120
aaggcaccca	aaagatggat	ttatgacaca	tccaaagtgg	cttctggagt	ccctgctcgc	180
ttcagtggca	gtgggtctgg	gaccgactac	tctctcacia	tcaacagctt	ggaggctgaa	240
gatgctgcca	cttattactg	ccaacagtgg	agtagtaacc	cgctcacgtt	cggtggcggg	300
accaaggtgg	agatcaaagg	cgaaggact	agtactgggt	ctggtggaag	tggagggttca	360
ggtggagcag	acgacgtcca	actggtgcag	tcaggggctg	aagtgaaaaa	acctggggcc	420
tcagtgaagg	tgtcctgcaa	ggcttctggc	tacaccttta	ctaggtagac	gatgcactgg	480
gtaaggcagg	cacctggaca	gggtctggaa	tggattggat	acattaatcc	tagccgtggt	540
tatactaatt	acaatcagaa	gttcaaggac	cgcgtcacia	tcactacaga	caaattccacc	600
agcacagcct	acatggaact	gagcagcctg	cggtctgagg	acactgcagt	ctattactgt	660
gcaagatatt	atgatgatca	ttactgcctt	gactactggg	gccaaggcac	cacggtcacc	720
gtctcctccg	gaggtgggtg	atcccagggtg	cagctgcagc	agtctggggc	tgagctgggtg	780
aggcctgggt	cctcagtga	gatttctctg	aaggcttctg	gctatgcatt	cagtagctac	840
tggatgaact	gggtgaagca	gaggcctgga	cagggtcttg	agtggattgg	acagatttgg	900
cctggagatg	gtgatactaa	ctacaatgga	aagttcaagg	gtaaagccac	tctgactgca	960
gacgaatcct	ccagcacagc	ctacatgcaa	ctcagcagcc	tagcatctga	ggactctgcg	1020
gtctatttct	gtgcaagacg	ggagactacg	acggtaggcc	gttattacta	tgctatggac	1080
tactggggcc	aagggaccac	ggtcaccgtc	tcctccgggtg	gtgggtggttc	tggcggcggc	1140
ggctccgggtg	gtgggtggttc	tgatatccag	ctgacccagt	ctccagcttc	tttggctgtg	1200
tctctagggc	agagggccac	catctcctgc	aaggccagcc	aaagtgttga	ttatgatggt	1260

gatagttatt tgaactggta ccaacagatt ccaggacagc cacccaaact cctcatctat 1320
gatgcatcca atctagtttc tgggatccca ccaggttta gtggcagtgg gtctgggaca 1380
gacttcaccc tcaacatcca tcctgtggag aaggtggatg ctgcaaccta tcaactgtcag 1440
caaagtactg aggatccgtg gacgttcggt ggagggacca agctcgagat caaa 1494

<210> 359

<211> 498

<212> PRT

<213> artificial sequence

<220>

<223> VL2VH7xCD19 LHHL

<400> 359

Asp Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
1 5 10 15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Tyr Met
20 25 30

Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr
35 40 45

Asp Thr Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
50 55 60

Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu
65 70 75 80

Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr
85 90 95

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Gly Glu Gly Thr Ser Thr
100 105 110

Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Val Gln Leu
115 120 125

Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val
130 135 140

Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp
145 150 155 160

Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn
165 170 175

Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe Lys Asp Arg Val
 180 185 190

Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser
 195 200 205

Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Tyr Tyr
 210 215 220

Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr
 225 230 235 240

Val Ser Ser Gly Gly Gly Gly Ser Gln Val Gln Leu Gln Gln Ser Gly
 245 250 255

Ala Glu Leu Val Arg Pro Gly Ser Ser Val Lys Ile Ser Cys Lys Ala
 260 265 270

Ser Gly Tyr Ala Phe Ser Ser Tyr Trp Met Asn Trp Val Lys Gln Arg
 275 280 285

Pro Gly Gln Gly Leu Glu Trp Ile Gly Gln Ile Trp Pro Gly Asp Gly
 290 295 300

Asp Thr Asn Tyr Asn Gly Lys Phe Lys Gly Lys Ala Thr Leu Thr Ala
 305 310 315 320

Asp Glu Ser Ser Ser Thr Ala Tyr Met Gln Leu Ser Ser Leu Ala Ser
 325 330 335

Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg Arg Glu Thr Thr Thr Val
 340 345 350

Gly Arg Tyr Tyr Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Thr Val
 355 360 365

Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
 370 375 380

Gly Gly Ser Asp Ile Gln Leu Thr Gln Ser Pro Ala Ser Leu Ala Val
 385 390 395 400

Ser Leu Gly Gln Arg Ala Thr Ile Ser Cys Lys Ala Ser Gln Ser Val
 405 410 415

Asp Tyr Asp Gly Asp Ser Tyr Leu Asn Trp Tyr Gln Gln Ile Pro Gly
 420 425 430

Gln Pro Pro Lys Leu Leu Ile Tyr Asp Ala Ser Asn Leu Val Ser Gly
 435 440 445

Ile Pro Pro Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu
450 455 377 460

Asn Ile His Pro Val Glu Lys Val Asp Ala Ala Thr Tyr His Cys Gln
465 470 475 480

Gln Ser Thr Glu Asp Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu Glu
485 490 495

Ile Lys

<210> 360

<211> 1497

<212> DNA

<213> artificial sequence

<220>

<223> VH7VL2xCD19 HLHL

<400> 360

gacgtccaac	tggtgcagtc	aggggctgaa	gtgaaaaaac	ctggggcctc	agtgaagggtg	60
tcctgcaagg	cttctggcta	cacctttact	aggtacacga	tgcactgggt	aaggcaggca	120
cctggacagg	gtctggaatg	gattggatac	attaatccta	gccgtgggtta	tactaattac	180
aatcagaagt	tcaaggaccg	cgtcacaatc	actacagaca	aatccaccag	cacagcctac	240
atggaactga	gcagcctgcg	ttctgaggac	actgcagtct	attactgtgc	aagatattat	300
gatgatcatt	actgccttga	ctactggggc	caaggcacca	cggtcaccgt	ctcctcaggc	360
gaagggtacta	gtactgggttc	tggtggaagt	ggagggttcag	gtggagcaga	cgacattgta	420
ctgacccagt	ctccagcaac	tctgtctctg	tctccagggg	agcgtgccac	cctgagctgc	480
agagccagtc	aaagtgtaag	ttacatgaac	tggtaccagc	agaagccggg	caaggcaccc	540
aaaagatgga	tttatgacac	atccaaagtg	gcttctggag	tccctgctcg	cttcagtggc	600
agtgggtctg	ggaccgacta	ctctctcaca	atcaacagct	tggaggctga	agatgctgcc	660
acttattact	gccaacagtg	gagtagtaac	ccgctcacgt	tcggtggcgg	gaccaagggtg	720
gagatcaaat	ccggagggtgg	tggatcccag	gtgcagctgc	agcagtctgg	ggctgagctg	780
gtgaggcctg	ggtcctcagt	gaagatttcc	tgcaaggctt	ctggctatgc	attcagtagc	840
tactggatga	actgggtgaa	gcagaggcct	ggacagggtc	ttgagtggat	tggacagatt	900
tggcctggag	atggtgatac	taactacaat	ggaaagttca	agggtaaagc	cactctgact	960
gcagacgaat	cctccagcac	agcctacatg	caactcagca	gcctagcatc	tgaggactct	1020
gcggtctatt	tctgtgcaag	acgggagact	acgacggtag	gccgttatta	ctatgctatg	1080
gactactggg	gccaagggac	cacggtcacc	gtctcctccg	gtgggtgggtg	ttctggcggc	1140

378

ggcggctccg gtggtggtgg ttctgatatc cagctgaccc agtctccagc ttctttggct	1200
gtgtctctag ggcagagggc caccatctcc tgcaaggcca gccaaagtgt tgattatgat	1260
ggtgatagtt atttgaactg gtaccaacag attccaggac agccacccaa actcctcatc	1320
tatgatgcat ccaatctagt ttctgggatc ccacccaggt ttagtggcag tgggtctggg	1380
acagacttca ccctcaacat ccacctgtg gagaagggtg atgctgcaac ctatcactgt	1440
cagcaaagta ctgaggatcc gtggacgttc ggtggaggga ccaagctcga gatcaaa	1497

<210> 361

<211> 499

<212> PRT

<213> artificial sequence

<220>

<223> VH7VL2xCD19 HLHL

<400> 361

Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr
20 25 30

Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe
50 55 60

Lys Asp Arg Val Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly
115 120 125

Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Val Leu Thr Gln Ser
130 135 140

Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys
145 150 155 160

Arg Ala Ser Gln Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro
 165 170 379 175
 Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser
 180 185 190
 Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser
 195 200 205
 Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys
 210 215 220
 Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
 225 230 235 240
 Glu Ile Lys Ser Gly Gly Gly Gly Ser Gln Val Gln Leu Gln Gln Ser
 245 250 255
 Gly Ala Glu Leu Val Arg Pro Gly Ser Ser Val Lys Ile Ser Cys Lys
 260 265 270
 Ala Ser Gly Tyr Ala Phe Ser Ser Tyr Trp Met Asn Trp Val Lys Gln
 275 280 285
 Arg Pro Gly Gln Gly Leu Glu Trp Ile Gly Gln Ile Trp Pro Gly Asp
 290 295 300
 Gly Asp Thr Asn Tyr Asn Gly Lys Phe Lys Gly Lys Ala Thr Leu Thr
 305 310 315 320
 Ala Asp Glu Ser Ser Ser Thr Ala Tyr Met Gln Leu Ser Ser Leu Ala
 325 330 335
 Ser Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg Arg Glu Thr Thr Thr
 340 345 350
 Val Gly Arg Tyr Tyr Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Thr
 355 360 365
 Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
 370 375 380
 Gly Gly Gly Ser Asp Ile Gln Leu Thr Gln Ser Pro Ala Ser Leu Ala
 385 390 395 400
 Val Ser Leu Gly Gln Arg Ala Thr Ile Ser Cys Lys Ala Ser Gln Ser
 405 410 415
 Val Asp Tyr Asp Gly Asp Ser Tyr Leu Asn Trp Tyr Gln Gln Ile Pro
 420 425 430
 Gly Gln Pro Pro Lys Leu Leu Ile Tyr Asp Ala Ser Asn Leu Val Ser

435 440 380 445
 Gly Ile Pro Pro Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr
 450 455 460
 Leu Asn Ile His Pro Val Glu Lys Val Asp Ala Ala Thr Tyr His Cys
 465 470 475 480
 Gln Gln Ser Thr Glu Asp Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu
 485 490 495

Glu Ile Lys

<210> 362
 <211> 1494
 <212> DNA
 <213> artificial sequence

<220>

<223> VL2VH7XCD19 LHLH

<400> 362
 gacattgtac tgaccagtc tccagcaact ctgtctctgt ctccagggga gcgtgccacc 60
 ctgagctgca gagccagtca aagtgttaagt tacatgaact ggtaccagca gaagccgggc 120
 aaggcaccga aaagatggat ttatgacaca tccaaagtgg cttctggagt ccctgctcgc 180
 ttcagtggca gtgggtctgg gaccgactac tctctcaca tcaacagctt ggaggctgaa 240
 gatgctgcca cttattactg ccaacagtgg agtagtaacc cgctcacgtt cggtggcggg 300
 accaaggtgg agatcaaagg cgaaggtact agtactgggt ctggtggaag tggagggttca 360
 ggtggagcag acgacgtcca actggtgcag tcaggggctg aagtgaaaaa acctggggcc 420
 tcagtgaagg tgtcctgcaa ggcttctggc tacaccttta ctaggtacac gatgcactgg 480
 gtaaggcagg cacctggaca gggctctggaa tggattggat acattaatcc tagccgtggg 540
 tatactaatt acaatcagaa gttcaaggac cgcgtcaca tctactacaga caaatccacc 600
 agcacagcct acatggaact gagcagcctg cgttctgagg aactgcagt ctattactgt 660
 gcaagatatt atgatgatca ttactgcctt gactactggg gccaaaggcac cacggtcacc 720
 gtctcctccg gaggtgggtg atccgatatc cagctgacct agtctccagc ttctttggct 780
 gtgtctctag ggcagagggc caccatctcc tgcaaggcca gccaaagtgt tgattatgat 840
 ggtgatagtt atttgaactg gtaccaacag attccaggac agccacccaa actcctcatc 900
 tatgatgcat ccaatctagt ttctgggatc ccaccaggt ttagtggcag tgggtctggg 960
 acagacttca ccctcaacat ccacctgtg gagaagggtg atgctgcaac ctatcactgt 1020
 cagcaaagta ctgaggatcc gtggacgttc ggtggaggga ccaagctcga gatcaaaggt 1080

ggtggtggtt ctggcggcgg cggctccggt ggtggtggtt ctcaggtgca gctgcagcag 1140
 tctggggctg agctggtgag gcctgggtcc tcagtgaaga tttcctgcaa ggcttctggc 1200
 tatgcattca gtagctactg gatgaactgg gtgaagcaga ggcctggaca gggctcttgag 1260
 tggattggac agatttggcc tggagatggt gatactaact acaatggaaa gttcaagggg 1320
 aaagccactc tgactgcaga cgaatcctcc agcacagcct acatgcaact cagcagccta 1380
 gcatctgagg actctgcggt ctatttctgt gcaagacggg agactacgac ggtaggccgt 1440
 tattactatg ctatggacta ctggggccaa gggaccacgg tcaccgtctc ctcc 1494

<210> 363

<211> 498

<212> PRT

<213> artificial sequence

<220>

<223> VL2VH7xCD19 LHLH

<400> 363

Asp Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
 1 5 10 15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Tyr Met
 20 25 30

Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr
 35 40 45

Asp Thr Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
 50 55 60

Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu
 65 70 75 80

Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr
 85 90 95

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Gly Glu Gly Thr Ser Thr
 100 105 110

Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Val Gln Leu
 115 120 125

Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val
 130 135 140

Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp

145	150	382 155	160
Val Arg Gln Ala	Pro Gly Gln Gly Leu	Glu Trp Ile Gly Tyr Ile Asn	
	165	170	175
Pro Ser Arg Gly Tyr Thr Asn Tyr	Asn Gln Lys Phe Lys Asp Arg Val		
	180	185	190
Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser			
	195	200	205
Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Tyr Tyr			
	210	215	220
Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr			
	225	230	235
Val Ser Ser Gly Gly Gly Gly Ser Asp Ile Gln Leu Thr Gln Ser Pro			
	245	250	255
Ala Ser Leu Ala Val Ser Leu Gly Gln Arg Ala Thr Ile Ser Cys Lys			
	260	265	270
Ala Ser Gln Ser Val Asp Tyr Asp Gly Asp Ser Tyr Leu Asn Trp Tyr			
	275	280	285
Gln Gln Ile Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr Asp Ala Ser			
	290	295	300
Asn Leu Val Ser Gly Ile Pro Pro Arg Phe Ser Gly Ser Gly Ser Gly			
	305	310	315
Thr Asp Phe Thr Leu Asn Ile His Pro Val Glu Lys Val Asp Ala Ala			
	325	330	335
Thr Tyr His Cys Gln Gln Ser Thr Glu Asp Pro Trp Thr Phe Gly Gly			
	340	345	350
Gly Thr Lys Leu Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly			
	355	360	365
Ser Gly Gly Gly Gly Ser Gln Val Gln Leu Gln Gln Ser Gly Ala Glu			
	370	375	380
Leu Val Arg Pro Gly Ser Ser Val Lys Ile Ser Cys Lys Ala Ser Gly			
	385	390	395
Tyr Ala Phe Ser Ser Tyr Trp Met Asn Trp Val Lys Gln Arg Pro Gly			
	405	410	415
Gln Gly Leu Glu Trp Ile Gly Gln Ile Trp Pro Gly Asp Gly Asp Thr			
	420	425	430

Asn Tyr Asn Gly Lys Phe Lys Gly Lys Ala Thr Leu Thr Ala Asp Glu
435 440 445

Ser Ser Ser Thr Ala Tyr Met Gln Leu Ser Ser Leu Ala Ser Glu Asp
450 455 460

Ser Ala Val Tyr Phe Cys Ala Arg Arg Glu Thr Thr Thr Val Gly Arg
465 470 475 480

Tyr Tyr Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val
485 490 495

Ser Ser

<210> 364

<211> 1497

<212> DNA

<213> artificial sequence

<220>

<223> VH7VL2xCD19 HLLH

<400> 364

gacgtccaac	tggtgcagtc	aggggctgaa	gtgaaaaaac	ctggggcctc	agtgaaggtg	60
tcctgcaagg	cttctggcta	cacctttact	aggtacacga	tgcactgggt	aaggcaggca	120
cctggacagg	gtctggaatg	gattggatac	attaatccta	gccgtgggta	tactaattac	180
aatcagaagt	tcaaggaccg	cgtcacaatc	actacagaca	aatccaccag	cacagcctac	240
atggaactga	gcagcctgcg	ttctgaggac	actgcagtct	attactgtgc	aagatattat	300
gatgatcatt	actgccttga	ctactggggc	caaggcacca	cggtcaccgt	ctcctcaggc	360
gaaggtacta	gtactggttc	tggtggaagt	ggaggttcag	gtggagcaga	cgacattgta	420
ctgacccagt	ctccagcaac	tctgtctctg	tctccagggg	agcgtgccac	cctgagctgc	480
agagccagtc	aaagtgtaag	ttacatgaac	tggtaccagc	agaagccggg	caaggcaccc	540
aaaagatgga	tttatgacac	atccaaagtg	gcttctggag	tccctgctcg	cttcagtggc	600
agtgggtctg	ggaccgacta	ctctctcaca	atcaacagct	tggaggctga	agatgctgcc	660
acttattact	gccaacagtg	gagtagtaac	ccgctcacgt	tcggtggcgg	gaccaaggtg	720
gagatcaa	at ccggagg	tggatccgat	atccagctga	cccagctctc	agcttctttg	780
gctgtgtctc	tagggcagag	ggccaccatc	tcctgcaagg	ccagccaaag	tgttgattat	840
gatggtgata	gttatttgaa	ctggtaccaa	cagattccag	gacagccacc	caaactcctc	900
atctatgatg	catccaatct	agtttctggg	atcccaccca	ggtttagtgg	cagtgggtct	960

384

gggacagact tcaccctcaa catccatcct gtggagaagg tggatgctgc aacctatcac	1020
tgtcagcaaa gtactgagga tccgtggacg ttcggtggag ggaccaagct cgagatcaaa	1080
ggtggtggtg gttctggcgg cggcggctcc ggtggtggtg gttctcaggt gcagctgcag	1140
cagtctgggg ctgagctggt gaggcctggg tcctcagtga agatttcctg caaggcttct	1200
ggctatgcat tcagtagcta ctggatgaac tgggtgaagc agaggcctgg acagggctct	1260
gagtggattg gacagatttg gcctggagat ggtgatacta actacaatgg aaagttcaag	1320
ggtaaagcca ctctgactgc agacgaatcc tccagcacag cctacatgca actcagcagc	1380
ctagcatctg aggactctgc ggtctatttc tgtgcaagac gggagactac gacggtaggc	1440
cgttattact atgctatgga ctactggggc caagggacca cggtcaccgt ctcctcc	1497

<210> 365

<211> 499

<212> PRT

<213> artificial sequence

<220>

<223> VH7VL2xCD19 HLLH

<400> 365

Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr
20 25 30

Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe
50 55 60

Lys Asp Arg Val Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly
115 120 125

Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Val Leu Thr Gln Ser
130 135 140

Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys
 145 150 155 160
 Arg Ala Ser Gln Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro
 165 170 175
 Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser
 180 185 190
 Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser
 195 200 205
 Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys
 210 215 220
 Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
 225 230 235 240
 Glu Ile Lys Ser Gly Gly Gly Gly Ser Asp Ile Gln Leu Thr Gln Ser
 245 250 255
 Pro Ala Ser Leu Ala Val Ser Leu Gly Gln Arg Ala Thr Ile Ser Cys
 260 265 270
 Lys Ala Ser Gln Ser Val Asp Tyr Asp Gly Asp Ser Tyr Leu Asn Trp
 275 280 285
 Tyr Gln Gln Ile Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr Asp Ala
 290 295 300
 Ser Asn Leu Val Ser Gly Ile Pro Pro Arg Phe Ser Gly Ser Gly Ser
 305 310 315 320
 Gly Thr Asp Phe Thr Leu Asn Ile His Pro Val Glu Lys Val Asp Ala
 325 330 335
 Ala Thr Tyr His Cys Gln Gln Ser Thr Glu Asp Pro Trp Thr Phe Gly
 340 345 350
 Gly Gly Thr Lys Leu Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly Gly
 355 360 365
 Gly Ser Gly Gly Gly Gly Ser Gln Val Gln Leu Gln Gln Ser Gly Ala
 370 375 380
 Glu Leu Val Arg Pro Gly Ser Ser Val Lys Ile Ser Cys Lys Ala Ser
 385 390 395 400
 Gly Tyr Ala Phe Ser Ser Tyr Trp Met Asn Trp Val Lys Gln Arg Pro
 405 410 415

Gly Gln Gly Leu Glu Trp Ile Gly Gln Ile Trp Pro Gly Asp Gly Asp
 420 425 430

Thr Asn Tyr Asn Gly Lys Phe Lys Gly Lys Ala Thr Leu Thr Ala Asp
 435 440 445

Glu Ser Ser Ser Thr Ala Tyr Met Gln Leu Ser Ser Leu Ala Ser Glu
 450 455 460

Asp Ser Ala Val Tyr Phe Cys Ala Arg Arg Glu Thr Thr Thr Val Gly
 465 470 475 480

Arg Tyr Tyr Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr
 485 490 495

Val Ser Ser

<210> 366

<211> 1494

<212> DNA

<213> artificial sequence

<220>

<223> VL3VH7xCD19 LHHL

<400> 366

gacattgtac tgaccagtc tccagcaact ctgtctctgt ctccagggga gcgtgccacc	60
ctgacctgca gagccagttc aagtgtaagt tacatgaact ggtaccagca gaagccgggc	120
aaggcaccga aaagatggat ttatgacaca tccaaagtgg cttctggagt ccctgctcgc	180
ttcagtggca gtgggtctgg gaccgactac tctctcaca tcaacagctt ggaggctgaa	240
gatgctgcca cttattactg ccaacagtgg agtagtaacc cgctcacgtt cggtggcggg	300
accaaggtgg agatcaaagg cgaaggtact agtactgggt ctggtggaag tggaggttca	360
gggtggagcag acgacgtcca actggtgcag tcaggggctg aagtgaaaaa acctggggcc	420
tcagtgaagg tgtcctgcaa ggcttctggc tacaccttta ctaggtacac gatgcactgg	480
gtaaggcagg cacctggaca gggctctggaa tggattggat acattaatcc tagccgtggt	540
tatactaatt acaatcagaa gttcaaggac cgcgtcaca tcactacaga caaatccacc	600
agcacagcct acatggaact gagcagcctg cgttctgagg aactgcagt ctattactgt	660
gcaagatatt atgatgatca ttactgcctt gactactggg gccaaaggcac cacggtcacc	720
gtctcctccg gaggtgggtg atcccagggtg cagctgcagc agtctggggc tgagctggtg	780
aggcctgggt cctcagtga gatttcctgc aaggcttctg gctatgcatt cagtagctac	840
tggtatgaact ggggtgaagca gaggcctgga cagggtcttg agtggattgg acagatttgg	900

cctggagatg gtgatactaa ctacaatgga aagttcaagg gtaaagccac tctgactgca 960
 gacgaatcct ccagcacagc ctacatgcaa ctcagcagcc tagcatctga ggactctgcg 1020
 gtctatttct gtgcaagacg ggagactacg acggtaggcc gttattacta tgctatggac 1080
 tactggggcc aagggaccac ggtcaccgtc tcctccggtg gtggtggttc tggcggcggc 1140
 ggctccggtg gtggtggttc tgatatccag ctgacccagt ctccagcttc tttggctgtg 1200
 tctctagggc agagggccac catctcctgc aaggccagcc aaagtgttga ttatgatggt 1260
 gatagttatt tgaactggta ccaacagatt ccaggacagc cacccaaact cctcatctat 1320
 gatgcatcca atctagtttc tgggatccca cccaggttta gtggcagtgg gtctgggaca 1380
 gacttcaccc tcaacatcca tcctgtggag aaggtggatg ctgcaaccta tcactgtcag 1440
 caaagtactg aggatccgtg gacgttcggt ggagggacca agctcgagat caaa 1494

<210> 367

<211> 498

<212> PRT

<213> artificial sequence

<220>

<223> VL3VH7xCD19 LHHL

<400> 367

Asp Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
 1 5 10 15

Glu Arg Ala Thr Leu Thr Cys Arg Ala Ser Ser Ser Val Ser Tyr Met
 20 25 30

Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr
 35 40 45

Asp Thr Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
 50 55 60

Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu
 65 70 75 80

Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr
 85 90 95

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Gly Glu Gly Thr Ser Thr
 100 105 110

Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Val Gln Leu
 115 120 125

Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val
 130 135 140

Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp
 145 150 155 160

Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn
 165 170 175

Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe Lys Asp Arg Val
 180 185 190

Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser
 195 200 205

Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Tyr Tyr
 210 215 220

Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr
 225 230 235 240

Val Ser Ser Gly Gly Gly Gly Ser Gln Val Gln Leu Gln Gln Ser Gly
 245 250 255

Ala Glu Leu Val Arg Pro Gly Ser Ser Val Lys Ile Ser Cys Lys Ala
 260 265 270

Ser Gly Tyr Ala Phe Ser Ser Tyr Trp Met Asn Trp Val Lys Gln Arg
 275 280 285

Pro Gly Gln Gly Leu Glu Trp Ile Gly Gln Ile Trp Pro Gly Asp Gly
 290 295 300

Asp Thr Asn Tyr Asn Gly Lys Phe Lys Gly Lys Ala Thr Leu Thr Ala
 305 310 315 320

Asp Glu Ser Ser Ser Thr Ala Tyr Met Gln Leu Ser Ser Leu Ala Ser
 325 330 335

~~Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg Arg Glu Thr Thr Thr Val~~
 340 345 350

Gly Arg Tyr Tyr Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Thr Val
 355 360 365

Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
 370 375 380

Gly Gly Ser Asp Ile Gln Leu Thr Gln Ser Pro Ala Ser Leu Ala Val
 385 390 395 400

Ser Leu Gly Gln Arg Ala Thr Ile Ser Cys³⁸⁹ Lys Ala Ser Gln Ser Val
 405 410 415
 Asp Tyr Asp Gly Asp Ser Tyr Leu Asn Trp Tyr Gln Gln Ile Pro Gly
 420 425 430
 Gln Pro Pro Lys Leu Leu Ile Tyr Asp Ala Ser Asn Leu Val Ser Gly
 435 440 445
 Ile Pro Pro Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu
 450 455 460
 Asn Ile His Pro Val Glu Lys Val Asp Ala Ala Thr Tyr His Cys Gln
 465 470 475 480
 Gln Ser Thr Glu Asp Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu Glu
 485 490 495

Ile Lys

<210> 368

<211> 1497

<212> DNA

<213> artificial sequence

<220>

<223> VH7VL3xCD19 HLHL

<400> 368

gacgtccaac tgggtgcagtc aggggctgaa gtgaaaaaac ctggggcctc agtgaaggtg	60
tcctgcaagg cttctggcta cacctttact aggtacacga tgcactgggt aaggcaggca	120
cctggacagg gtctggaatg gattggatac attaatccta gccgtgggta tactaattac	180
aatcagaagt tcaaggaccg cgtcacaatc actacagaca aatccaccag cacagcctac	240
atggaactga gcagcctgcg ttctgaggac actgcagtct attactgtgc aagatattat	300
gatgatcatt actgccttga ctactggggc caaggcacca cggtcaccgt ctctcaggc	360
gaaggtacta gtactggttc tgggtggaagt ggaggttcag gtggagcaga cgacattgta	420
ctgacccagt ctccagcaac tctgtctctg tctccagggg agcgtgccac cctgacctgc	480
agagccagtt caagtgtaag ttacatgaac tggtagcagc agaagccggg caaggcacc	540
aaaagatgga tttatgacac atccaaagtg gcttctggag tccctgctcg cttcagtggc	600
agtgggtctg ggaccgacta ctctctcaca atcaacagct tggaggctga agatgctgcc	660
acttattact gccaacagtg gagtagtaac ccgctcacgt tcggtggcgg gaccaaggtg	720
gagatcaaat ccggagggtg tggatcccag gtgcagctgc agcagtctgg ggctgagctg	780

390

gtgaggcctg ggtcctcagt gaagatttcc tgcaaggcctt ctggctatgc attcagtagc	840
tactggatga actgggtgaa gcagaggcct ggacagggtc ttgagtggat tggacagatt	900
tggcctggag atggtgatac taactacaat ggaaagttca agggtaaagc cactctgact	960
gcagacgaat cctccagcac agcctacatg caactcagca gcctagcatc tgaggactct	1020
gcggtctatt tctgtgcaag acgggagact acgacggtag gccgttatta ctatgctatg	1080
gactactggg gccaaaggac cacggtcacc gtctcctccg gtggtggtgg ttctggcggc	1140
ggcggctccg gtggtggtgg ttctgatatc cagctgaccc agtctccagc ttctttggct	1200
gtgtctctag ggcagagggc caccatctcc tgcaaggcca gccaaagtgt tgattatgat	1260
ggtgatagtt atttgaactg gtaccaacag attccaggac agccacccaa actcctcatc	1320
tatgatgcat ccaatctagt ttctgggatc ccacccaggt ttagtggcag tgggtctggg	1380
acagacttca ccctcaacat ccatcctgtg gagaagggtgg atgctgcaac ctatcactgt	1440
cagcaaagta ctgaggatcc gtggacgttc ggtggagggga ccaagctcga gatcaaa	1497

<210> 369

<211> 499

<212> PRT

<213> artificial sequence

<220>

<223> VH7VL3xCD19 HLHL

<400> 369

Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr
20 25 30

Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe
50 55 60

Lys Asp Arg Val Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly
 115 120 125³⁹¹

Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Val Leu Thr Gln Ser
 130 135 140

Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Thr Cys
 145 150 155 160

Arg Ala Ser Ser Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro
 165 170 175

Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser
 180 185 190

Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser
 195 200 205

Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys
 210 215 220

Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
 225 230 235 240

Glu Ile Lys Ser Gly Gly Gly Gly Ser Gln Val Gln Leu Gln Gln Ser
 245 250 255

Gly Ala Glu Leu Val Arg Pro Gly Ser Ser Val Lys Ile Ser Cys Lys
 260 265 270

Ala Ser Gly Tyr Ala Phe Ser Ser Tyr Trp Met Asn Trp Val Lys Gln
 275 280 285

Arg Pro Gly Gln Gly Leu Glu Trp Ile Gly Gln Ile Trp Pro Gly Asp
 290 295 300

Gly Asp Thr Asn Tyr Asn Gly Lys Phe Lys Gly Lys Ala Thr Leu Thr
 305 310 315 320

Ala Asp Glu Ser Ser Ser Thr Ala Tyr Met Gln Leu Ser Ser Leu Ala
 325 330 335

Ser Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg Arg Glu Thr Thr Thr
 340 345 350

Val Gly Arg Tyr Tyr Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Thr
 355 360 365

Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
 370 375 380

Gly Gly Gly Ser Asp Ile Gln Leu Thr Gln Ser Pro Ala Ser Leu Ala

gtctcctccg gaggtggtgg atccgatatc cagctgaccc agtctccagc ttcttttggt 780
 gtgtctctag ggcagagggc caccatctcc tgcaaggcca gccaaagtgt tgattatgat 840
 ggtgatagtt atttgaactg gtaccaacag attccaggac agccacccaa actcctcatc 900
 tatgatgcat ccaatctagt ttctgggatc ccacccaggt ttagtggcag tgggtctggg 960
 acagacttca ccctcaacat ccatcctgtg gagaaggtgg atgctgcaac ctatcactgt 1020
 cagcaaagta ctgaggatcc gtggacgttc ggtggaggga ccaagctcga gatcaaaggt 1080
 ggtggtggtt ctggcggcgg cggctccggt ggtggtggtt ctcaggtgca gctgcagcag 1140
 tctggggctg agctggtgag gcctgggtcc tcagtgaaga tttcctgcaa ggcttctggc 1200
 tatgcattca gtagctactg gatgaactgg gtgaagcaga ggcctggaca gggctcttgag 1260
 tggattggac agatttggcc tggagatggt gatactaact acaatggaaa gttcaagggt 1320
 aaagccactc tgactgcaga cgaatcctcc agcacagcct acatgcaact cagcagccta 1380
 gcatctgagg actctgcggt ctatttctgt gcaagacggg agactacgac ggtaggccgt 1440
 tattactatg ctatggacta ctggggccaa gggaccacgg tcaccgtctc ctcc 1494

<210> 371

<211> 498

<212> PRT

<213> artificial sequence

<220>

<223> VL3VH7xCD19 LHLH

<400> 371

Asp Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
1 5 10 15

Glu Arg Ala Thr Leu Thr Cys Arg Ala Ser Ser Ser Val Ser Tyr Met
20 25 30

Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr
35 40 45

Asp Thr Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
50 55 60

Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu
65 70 75 80

Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr
85 90 95

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Gly Glu Gly Thr Ser Thr

[illegible]

Leu Val Arg Pro Gly Ser Ser Val Lys Ile Ser Cys Lys Ala Ser Gly
385 390 395 400

Tyr Ala Phe Ser Ser Tyr Trp Met Asn Trp Val Lys Gln Arg Pro Gly
405 410 415

Gln Gly Leu Glu Trp Ile Gly Gln Ile Trp Pro Gly Asp Gly Asp Thr
420 425 430

Asn Tyr Asn Gly Lys Phe Lys Gly Lys Ala Thr Leu Thr Ala Asp Glu
435 440 445

Ser Ser Ser Thr Ala Tyr Met Gln Leu Ser Ser Leu Ala Ser Glu Asp
450 455 460

Ser Ala Val Tyr Phe Cys Ala Arg Arg Glu Thr Thr Thr Val Gly Arg
465 470 475 480

Tyr Tyr Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val
485 490 495

Ser Ser

<210> 372

<211> 1497

<212> DNA

<213> artificial sequence

<220>

<223> VH7VL3xCD19 HLLH

<400> 372

gacgtccaac tgggtgcagtc aggggctgaa gtgaaaaaac ctggggcctc agtgaagggtg	60
tcctgcaagg cttctggcta cacctttact aggtacacga tgcactgggt aaggcaggca	120
cctggacagg gtctggaatg gattggatac attaataccta gccgtgggtta tactaattac	180
aatcagaagt tcaaggaccg cgtcacaatc actacagaca aatccaccag cacagcctac	240
atggaactga gcagcctgcg ttctgaggac actgcagtct attactgtgc aagatattat	300
gatgatcatt actgccttga ctactggggc caaggcacca cggtcaccgt ctctcaggc	360
gaagggtacta gtactgggttc tgggtggaagt ggagggttcag gtggagcaga cgacattgta	420
ctgacccagt ctccagcaac tctgtctctg tctccagggg agcgtgccac cctgacctgc	480
agagccagtt caagtgtaag ttacatgaac tgggtaccagc agaagccggg caaggcaccc	540
aaaagatgga tttatgacac atccaaagtg gcttctggag tccctgctcg cttcagtggc	600

396

agtgggtctg ggaccgacta ctctctcaca atcaacagct tggaggctga agatgctgcc	660
acttattact gccaacagtg gagtagtaac ccgctcacgt tcggtggcgg gaccaagggtg	720
gagatcaaat ccggagggtgg tggatccgat atccagctga cccagtctcc agcttctttg	780
gctgtgtctc tagggcagag ggccaccatc tcctgcaagg ccagccaaag tgttgattat	840
gatggtgata gttatttgaa ctggtaccaa cagattccag gacagccacc caaactcctc	900
atctatgatg catccaatct agtttctggg atcccaccca ggtttaagtgg cagtgggtct	960
gggacagact tcaccctcaa catccatcct gtggagaagg tggatgctgc aacctatcac	1020
tgtcagcaaa gtactgagga tccgtggacg ttcggtggag ggaccaagct cgagatcaaa	1080
ggtggtggtg gttctggcgg cggcggctcc ggtggtggtg gttctcaggt gcagctgcag	1140
cagtctgggg ctgagctggt gaggcctggg tcctcagtga agatttcctg caaggcttct	1200
ggctatgcat tcagtagcta ctggatgaac tgggtgaagc agaggcctgg acagggtctt	1260
gagtggattg gacagatttg gcctggagat ggtgatacta actacaatgg aaagttcaag	1320
ggtaaagcca ctctgactgc agacgaatcc tccagcacag cctacatgca actcagcagc	1380
ctagcatctg aggactctgc ggtctatttc tgtgcaagac gggagactac gacggtaggc	1440
cgttattact atgctatgga ctactggggc caagggacca cggtcaccgt ctcctcc	1497

<210> 373

<211> 499

<212> PRT

<213> artificial sequence

<220>

<223> VH7VL3xCD19 HLLH

<400> 373

Asp	Val	Gln	Leu	Val	Gln	Ser	Gly	Ala	Glu	Val	Lys	Lys	Pro	Gly	Ala
1				5					10					15	

Ser	Val	Lys	Val	Ser	Cys	Lys	Ala	Ser	Gly	Tyr	Thr	Phe	Thr	Arg	Tyr
			20					25					30		

Thr	Met	His	Trp	Val	Arg	Gln	Ala	Pro	Gly	Gln	Gly	Leu	Glu	Trp	Ile
		35					40					45			

Gly	Tyr	Ile	Asn	Pro	Ser	Arg	Gly	Tyr	Thr	Asn	Tyr	Asn	Gln	Lys	Phe
	50					55					60				

Lys	Asp	Arg	Val	Thr	Ile	Thr	Thr	Asp	Lys	Ser	Thr	Ser	Thr	Ala	Tyr
65					70					75					80

Met	Glu	Leu	Ser	Ser	Leu	Arg	Ser	Glu	Asp	Thr	Ala	Val	Tyr	Tyr	Cys
				85					90					95	

Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
 100 105 110
 Thr Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly
 115 120 125
 Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Val Leu Thr Gln Ser
 130 135 140
 Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Thr Cys
 145 150 155 160
 Arg Ala Ser Ser Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro
 165 170 175
 Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser
 180 185 190
 Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser
 195 200 205
 Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys
 210 215 220
 Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
 225 230 235 240
 Glu Ile Lys Ser Gly Gly Gly Gly Ser Asp Ile Gln Leu Thr Gln Ser
 245 250 255
 Pro Ala Ser Leu Ala Val Ser Leu Gly Gln Arg Ala Thr Ile Ser Cys
 260 265 270
 Lys Ala Ser Gln Ser Val Asp Tyr Asp Gly Asp Ser Tyr Leu Asn Trp
 275 280 285
 Tyr Gln Gln Ile Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr Asp Ala
 290 295 300
 Ser Asn Leu Val Ser Gly Ile Pro Pro Arg Phe Ser Gly Ser Gly Ser
 305 310 315 320
 Gly Thr Asp Phe Thr Leu Asn Ile His Pro Val Glu Lys Val Asp Ala
 325 330 335
 Ala Thr Tyr His Cys Gln Gln Ser Thr Glu Asp Pro Trp Thr Phe Gly
 340 345 350
 Gly Gly Thr Lys Leu Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly Gly
 355 360 365

398

Gly Ser Gly Gly Gly Gly Ser Gln Val Gln Leu Gln Gln Ser Gly Ala
370 375 380

Glu Leu Val Arg Pro Gly Ser Ser Val Lys Ile Ser Cys Lys Ala Ser
385 390 395 400

Gly Tyr Ala Phe Ser Ser Tyr Trp Met Asn Trp Val Lys Gln Arg Pro
405 410 415

Gly Gln Gly Leu Glu Trp Ile Gly Gln Ile Trp Pro Gly Asp Gly Asp
420 425 430

Thr Asn Tyr Asn Gly Lys Phe Lys Gly Lys Ala Thr Leu Thr Ala Asp
435 440 445

Glu Ser Ser Ser Thr Ala Tyr Met Gln Leu Ser Ser Leu Ala Ser Glu
450 455 460

Asp Ser Ala Val Tyr Phe Cys Ala Arg Arg Glu Thr Thr Thr Val Gly
465 470 475 480

Arg Tyr Tyr Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr
485 490 495

Val Ser Ser

<210> 374

<211> 1497

<212> DNA

<213> artificial sequence

<220>

<223> CD19xVH5/VL1 HLHL

<400> 374	
caggtgcagc tgcagcagtc tggggctgag ctggtgaggc ctgggtcctc agtgaagatt	60
tcctgcaagg cttctggcta tgcattcagt agctactgga tgaactgggt gaagcagagg	120
cctggacagg gtcttgagtg gattggacag atttggcctg gagatggtga tactaactac	180
aatggaaagt tcaagggtaa agccactctg actgcagacg aatcctccag cacagcctac	240
atgcaactca gcagcctagc atctgaggac tctgcggtct atttctgtgc aagacgggag	300
actacgacgg taggccgtta ttactatgct atggactact ggggcccaagg gaccacggtc	360
accgtctcct ccggtggtgg tggttctggc ggcggcggct ccggtggtgg tggttctgat	420
atccagctga cccagtctcc agcttctttg gctgtgtctc tagggcagag ggccaccatc	480
tcctgcaagg ccagccaaag tgttgattat gatggtgata gttatttgaa ctggtaccaa	540

cagattccag gacagccacc caaactcctc atctatgatg catccaatct agttttctggg 600
 atccccacca ggttttagtgg cagtgggtct gggacagact tcaccctcaa catccatcct 660
 gtggagaagg tggatgctgc aacctatcac tgtcagcaaa gtactgagga tccgtggacg 720
 ttcggtggag ggaccaagct cgagatcaaa tccggaggtg gtggatccga cgtccaactg 780
 gtgcagtcag gggctgaagt gaaaaaacct ggggcctcag tgaagggtgtc ctgcaaggct 840
 tctggctaca cttttactag gtacacgatg cactgggtaa ggcaggcacc tggacagggt 900
 ctggaatgga ttggatacat taatcctagc cgtgggttata ctaattacgc agacagcgtc 960
 aagggccgct tcacaatcac tacagacaaa tccaccagca cagcctacat ggaactgagc 1020
 agcctgcggt ctgaggacac tgcaacctat tactgtgcaa gatattatga tgatcattac 1080
 tgccttgact actggggcca aggcaccacg gtcaccgtct cctcaggcga aggtactagt 1140
 actggttctg gtggaagtgg aggttcaggt ggagcagacg acattcagat gaccagctct 1200
 ccatctagcc tgtctgcatc tgtcggggac cgtgtcacca tcacctgcag agccagtcaa 1260
 agtgtaagtt acatgaactg gtaccagcag aagccgggca aggcaccaa aagatggatt 1320
 tatgacacat ccaaagtggc ttctggagtc cctgctcgct tcagtggcag tgggtctggg 1380
 accgactact ctctcacaat caacagcttg gaggtgaag atgctgccac ttattactgc 1440
 caacagtgga gtagtaaccc gctcacgttc ggtggcggga ccaagggtgga gatcaaa 1497

<210> 375

<211> 499

<212> PRT

<213> artificial sequence

<220>

<223> CD19xVH5VL1 HLHL

<400> 375

Gln Val Gln Leu Gln Gln Ser Gly Ala Glu Leu Val Arg Pro Gly Ser
 1 5 10 15

Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Ser Ser Tyr
 20 25 30

Trp Met Asn Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile
 35 40 45

Gly Gln Ile Trp Pro Gly Asp Gly Asp Thr Asn Tyr Asn Gly Lys Phe
 50 55 60

Lys Gly Lys Ala Thr Leu Thr Ala Asp Glu Ser Ser Ser Thr Ala Tyr
 65 70 75 80

400

Met Gln Leu Ser Ser Leu Ala Ser Glu Asp Ser Ala Val Tyr Phe Cys
85 90 95

Ala Arg Arg Glu Thr Thr Thr Val Gly Arg Tyr Tyr Tyr Ala Met Asp
100 105 110

Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly
115 120 125

ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Gln Leu Thr
130 135 140

Gln Ser Pro Ala Ser Leu Ala Val Ser Leu Gly Gln Arg Ala Thr Ile
145 150 155 160

Ser Cys Lys Ala Ser Gln Ser Val Asp Tyr Asp Gly Asp Ser Tyr Leu
165 170 175

Asn Trp Tyr Gln Gln Ile Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr
180 185 190

Asp Ala Ser Asn Leu Val Ser Gly Ile Pro Pro Arg Phe Ser Gly Ser
195 200 205

Gly Ser Gly Thr Asp Phe Thr Leu Asn Ile His Pro Val Glu Lys Val
210 215 220

Asp Ala Ala Thr Tyr His Cys Gln Gln Ser Thr Glu Asp Pro Trp Thr
225 230 235 240

Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Ser Gly Gly Gly Gly Ser
245 250 255

Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
260 265 270

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr
275 280 285

Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
290 295 300

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val
305 310 315 320

Lys Gly Arg Phe Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr
325 330 335

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys
340 345 350

Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
 355 360 401 365
 Thr Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly
 370 375 380
 Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Gln Met Thr Gln Ser
 385 390 395 400
 Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys
 405 410 415
 Arg Ala Ser Gln Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro
 420 425 430
 Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser
 435 440 445
 Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser
 450 455 460
 Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys
 465 470 475 480
 Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
 485 490 495

Glu Ile Lys

<210> 376

<211> 1494

<212> DNA

<213> artificial sequence

<220>

<223> CD19xVL1VH5 LHLH

<400> 376

gatatccagc tgacccagtc tccagcttct ttggctgtgt ctctagggca gagggccacc	60
atctcctgca aggccagcca aagtgttgat tatgatggtg atagttatatt gaactggtac	120
caacagattc caggacagcc acccaaactc ctcatctatg atgcatccaa tctagtttct	180
gggatccac ccaggtttag tggcagtggg tctgggacag acttcaccct caacatccat	240
cctgtggaga aggtggatgc tgcaacctat cactgtcagc aaagtactga ggatccgtgg	300
acgttcggtg gagggaccaa gctcgagatc aaagggtggtg gtggttcttg cggcggcggc	360
tccggtggtg gtggttctca ggtgcagctg cagcagtctg gggctgagct ggtgaggcct	420

402

gggtcctcag tgaagatttc ctgcaaggct tctggctatg cattcagtag ctactggatg	480
aactgggtga agcagaggcc tggacagggt cttgagtga ttggacagat ttggcctgga	540
gatggtgata ctaactacaa tggaaagtcc aagggtaaag ccactctgac tgcagacgaa	600
tcctccagca cagcctacat gcaactcagc agcctagcat ctgaggactc tgcggtctat	660
ttctgtgcaa gacgggagac tacgacggtg ggccgttatt actatgctat ggactactgg	720
ggccaaggga ccacgggtcac cgtctcctcc ggagggtggg gatccgacat tcagatgacc	780
cagtctccat ctagcctgtc tgcattctgtc ggggaccgtg tcaccatcac ctgcagagcc	840
agtcaaagtg taagttacat gaactgggtac cagcagaagc cgggcaaggc acccaaaaga	900
tggatttatg acacatccaa agtggcttct ggagtccttg ctgcgttcag tggcagtggg	960
tctgggaccg actactctct cacaatcaac agcttggagg ctgaagatgc tgccacttat	1020
tactgccaac agtggagtag taaccgctc acgttcggtg gcgggaccaa ggtggagatc	1080
aaaggcgaag gtactagtag tggttctggt ggaagtggag gttcaggtgg agcagacgac	1140
gtccaactgg tgcagtcagg ggctgaagtg aaaaaacctg gggcctcagt gaagggtgcc	1200
tgcaaggctt ctggctacac ctttactagg tacacgatgc actgggtaag gcaggcacct	1260
ggacaggggtc tggaatggat tggatacatt aatcctagcc gtgggttatac taattacgca	1320
gacagcgtca agggccgctt cacaatcact acagacaaat ccaccagcac agcctacatg	1380
gaactgagca gcctgcgttc tgaggacact gcaacctatt actgtgcaag atattatgat	1440
gatcattact gccttgacta ctggggccaa ggcaccacgg tcaccgtctc ctca	1494

<210> 377

<211> 498

<212> PRT

<213> artificial sequence

<220>

<223> CD19xVL1VH5 LHLH

<400> 377

----- Asp Ile Gln Leu Thr Gln Ser Pro Ala Ser Leu Ala Val Ser Leu Gly
1 5 10 15

Gln Arg Ala Thr Ile Ser Cys Lys Ala Ser Gln Ser Val Asp Tyr Asp
20 25 30

Gly Asp Ser Tyr Leu Asn Trp Tyr Gln Gln Ile Pro Gly Gln Pro Pro
35 40 45

Lys Leu Leu Ile Tyr Asp Ala Ser Asn Leu Val Ser Gly Ile Pro Pro
50 55 60

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp⁴⁰³ Phe Thr Leu Asn Ile His
 65 70 75 80
 Pro Val Glu Lys Val Asp Ala Ala Thr Tyr His Cys Gln Gln Ser Thr
 85 90 95
 Glu Asp Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Gly
 100 105 110
 Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Val
 115 120 125
 Gln Leu Gln Gln Ser Gly Ala Glu Leu Val Arg Pro Gly Ser Ser Val
 130 135 140
 Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Ser Ser Tyr Trp Met
 145 150 155 160
 Asn Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile Gly Gln
 165 170 175
 Ile Trp Pro Gly Asp Gly Asp Thr Asn Tyr Asn Gly Lys Phe Lys Gly
 180 185 190
 Lys Ala Thr Leu Thr Ala Asp Glu Ser Ser Ser Thr Ala Tyr Met Gln
 195 200 205
 Leu Ser Ser Leu Ala Ser Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg
 210 215 220
 Arg Glu Thr Thr Thr Val Gly Arg Tyr Tyr Tyr Ala Met Asp Tyr Trp
 225 230 235 240
 Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp
 245 250 255
 Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp
 260 265 270
 Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Ser Tyr Met Asn
 275 280 285
 Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp
 290 295 300
 Thr Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser Gly
 305 310 315 320
 Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp
 325 330 335
 Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe

340 345 404 350
 Gly Gly Gly Thr Lys Val Glu Ile Lys Gly Glu Gly Thr Ser Thr Gly
 355 360 365
 Ser Gly Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Val Gln Leu Val
 370 375 380
 Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val Ser
 385 390 395 400
 Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp Val
 405 410 415
 Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn Pro
 420 425 430
 Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr
 435 440 445
 Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser Ser
 450 455 460
 Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys Ala Arg Tyr Tyr Asp
 465 470 475 480
 Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val
 485 490 495
 Ser Ser

<210> 378

<211> 1497

<212> DNA

<213> artificial sequence

<220>

<223> CD19xVL1VH5 HLLH

<400> 378
 caggtgcagc tgcagcagtc tggggctgag ctggtgaggc ctgggtcctc agtgaagatt 60
 tcctgcaagg cttctggcta tgcattcagt agctactgga tgaactgggt gaagcagagg 120
 cctggacagg gtcttgagtg gattggacag atttggcctg gagatggtga tactaactac 180
 aatggaaagt tcaagggtaa agccactctg actgcagacg aatcctccag cacagcctac 240
 atgcaactca gcagcctagc atctgaggac tctgcggtct atttctgtgc aagacgggag 300
 actacgacgg taggccgtta ttactatgct atggactact ggggccaagg gaccacggtc 360


```

accgtctcct ccggtggtgg tggttctggc ggcggcggct ccggtggtgg tggttctgat 420
atccagctga cccagtctcc agcttctttg gctgtgtctc tagggcagag ggctaccatc 480
tcctgcaagg ccagccaaag tgttgattat gatggtgata gttatttgaa ctggtaccaa 540
cagattccag gacagccacc caaactcctc atctatgatg catccaatct agtttctggg 600
atcccaccca ggttttagtgg cagtgggtct gggacagact tcacctcaa catccatcct 660
gtggagaagg tggatgctgc aacctatcac tgtcagcaaa gtactgagga tccgtggacg 720
ttcgggtggag ggaccaagct cgagatcaaa tccggagggtg gtggatccga cattcagatg 780
acccagtctc catctagcct gtctgcatct gtcggggacc gtgtcaccat cacctgcaga 840
gccagtcaaa gtgtaagtta catgaactgg taccagcaga agccgggcaa ggcacccaaa 900
agatggattt atgacacatc caaagtggct tctggagtcc ctgctcgctt cagtggcagt 960
gggtctggga ccgactactc tctcacaatc aacagcttgg aggctgaaga tgctgccact 1020
tattactgcc aacagtggag tagtaaccgc ctcacgttcg gtggcgggac caaggtggag 1080
atcaaaggcg aaggtactag tactggttct ggtggaagtg gaggttcagg tggagcagac 1140
gacgtccaac tgggtgcagtc aggggctgaa gtgaaaaaac ctggggcctc agtgaagggtg 1200
tcctgcaagg cttctggcta cacctttact aggtacacga tgcactgggt aaggcaggca 1260
cctggacagg gtctggaatg gattggatac attaatccta gccgtgggtta tactaattac 1320
gcagacagcg tcaagggccg cttcacaatc actacagaca aatccaccag cacagcctac 1380
atggaactga gcagcctgcg ttctgaggac actgcaacct attactgtgc aagatattat 1440
gatgatcatt actgccttga ctactggggc caaggcacca cggtcaccgt ctcctca 1497

```

<210> 379

<211> 499

<212> PRT

<213> artificial sequence

<220>

<223> CD19xVL1VH5 HLLH

<400> 379

Gln Val Gln Leu Gln Gln Ser Gly Ala Glu Leu Val Arg Pro Gly Ser
1 5 10 15

Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Ser Ser Tyr
20 25 30

Trp Met Asn Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Gln Ile Trp Pro Gly Asp Gly Asp Thr Asn Tyr Asn Gly Lys Phe

50 55 406 60
 Lys Gly Lys Ala Thr Leu Thr Ala Asp Glu Ser Ser Ser Thr Ala Tyr
 65 70 75 80
 Met Gln Leu Ser Ser Leu Ala Ser Glu Asp Ser Ala Val Tyr Phe Cys
 85 90 95
 Ala Arg Arg Glu Thr Thr Thr Val Gly Arg Tyr Tyr Tyr Ala Met Asp
 100 105 110
 Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly
 115 120 125
 Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Gln Leu Thr
 130 135 140
 Gln Ser Pro Ala Ser Leu Ala Val Ser Leu Gly Gln Arg Ala Thr Ile
 145 150 155 160
 Ser Cys Lys Ala Ser Gln Ser Val Asp Tyr Asp Gly Asp Ser Tyr Leu
 165 170 175
 Asn Trp Tyr Gln Gln Ile Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr
 180 185 190
 Asp Ala Ser Asn Leu Val Ser Gly Ile Pro Pro Arg Phe Ser Gly Ser
 195 200 205
 Gly Ser Gly Thr Asp Phe Thr Leu Asn Ile His Pro Val Glu Lys Val
 210 215 220
 Asp Ala Ala Thr Tyr His Cys Gln Gln Ser Thr Glu Asp Pro Trp Thr
 225 230 235 240
 Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Ser Gly Gly Gly Gly Ser
 245 250 255
 Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
 260 265 270
 Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Ser Tyr Met
 275 280 285
 Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr
 290 295 300
 Asp Thr Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
 305 310 315 320
 Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu
 325 330 335

Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr
 340 345 350

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Gly Glu Gly Thr Ser Thr
 355 360 365

Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Val Gln Leu
 370 375 380

Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val
 385 390 395 400

Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp
 405 410 415

Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn
 420 425 430

Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val Lys Gly Arg Phe
 435 440 445

Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser
 450 455 460

Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys Ala Arg Tyr Tyr
 465 470 475 480

Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr
 485 490 495

Val Ser Ser

<210> 380

<211> 1497

<212> DNA

<213> artificial sequence

<220>

<223> CD19xVH5VL2 HLHL

<400> 380

cagggtgcagc tgcagcagtc tggggctgag ctggtgagggc ctgggtcctc agtgaagatt	60
tcctgcaagg cttctggcta tgcattcagt agctactgga tgaactgggt gaagcagagg	120
cctggacagg gtcttgagtg gattggacag atttggcctg gagatgggtga tactaactac	180
aatggaaagt tcaagggtaa agccactctg actgcagacg aatcctccag cacagcctac	240

408

atgcaactca gcagcctagc atctgaggac tctgcggtct atttctgtgc aagacgggag	300
actacgacgg taggccgtta ttactatgct atggactact ggggccaagg gaccacggtc	360
accgtctcct ccggtggtgg tggttctggc ggcggcggct ccggtggtgg tggttctgat	420
atccagctga cccagtctcc agcttctttg gctgtgtctc tagggcagag ggccaccatc	480
tcctgcaagg ccagccaaag tgttgattat gatggtgata gttatttgaa ctggtacca	540
cagattccag gacagccacc caaactcctc atctatgatg catccaatct agtttctggg	600
atcccaccca ggtttagtgg cagtgggtct gggacagact tcacctcaa catccatcct	660
gtggagaagg tggatgctgc aacctatcac tgtcagcaaa gtactgagga tccgtggacg	720
ttcgggtggag ggaccaagct cgagatcaaa tccggagggtg gtggatccga cgtccaactg	780
gtgcagtcag gggctgaagt gaaaaaacct ggggcctcag tgaagggtgc ctgcaaggct	840
tctggctaca cctttactag gtacacgatg cactgggtaa ggcaggcacc tggacagggg	900
ctggaatgga ttggatacat taatcctagc cgtgggtata ctaattacgc agacagcgtc	960
aagggccgct tcacaatcac tacagacaaa tccaccagca cagcctacat ggaactgagc	1020
agcctgcgtt ctgaggacac tgcaacctat tactgtgcaa gatattatga tgatcattac	1080
tgccttgact actggggcca aggcaccacg gtcaccgtct cctcaggcga aggtactagt	1140
actggttctg gtggaagtgg aggttcagggt ggagcagacg acattgtact gaccagtc	1200
ccagcaactc tgtctctgtc tccaggggag cgtgccaccc tgagctgcag agccagtcaa	1260
agtgtaagtt acatgaactg gtaccagcag aagccgggca aggcacccaa aagatggatt	1320
tatgacacat ccaaagtggc ttctggagtc cctgctcgct tcagtggcag tgggtctggg	1380
accgactact ctctcacaat caacagcttg gaggctgaag atgctgccac ttattactgc	1440
caacagtgga gtagtaaccc gctcacgttc ggtggcgggg ccaagggtgga gatcaaa	1497

<210> 381

<211> 499

<212> PRT

<213> artificial sequence

<220>

<223> CD19xVH5VL2 HLHL

<400> 381

Gln Val Gln Leu Gln Gln Ser Gly Ala Glu Leu Val Arg Pro Gly Ser
1 5 10 15

Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Ser Ser Tyr
20 25 30

Trp Met Asn Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Gln Ile Trp Pro Gly Asp Gly Asp Thr Asn Tyr Asn Gly Lys Phe
 50 55 60
 Lys Gly Lys Ala Thr Leu Thr Ala Asp Glu Ser Ser Ser Thr Ala Tyr
 65 70 75 80
 Met Gln Leu Ser Ser Leu Ala Ser Glu Asp Ser Ala Val Tyr Phe Cys
 85 90 95
 Ala Arg Arg Glu Thr Thr Thr Val Gly Arg Tyr Tyr Tyr Ala Met Asp
 100 105 110
 Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly
 115 120 125
 Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Gln Leu Thr
 130 135 140
 Gln Ser Pro Ala Ser Leu Ala Val Ser Leu Gly Gln Arg Ala Thr Ile
 145 150 155 160
 Ser Cys Lys Ala Ser Gln Ser Val Asp Tyr Asp Gly Asp Ser Tyr Leu
 165 170 175
 Asn Trp Tyr Gln Gln Ile Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr
 180 185 190
 Asp Ala Ser Asn Leu Val Ser Gly Ile Pro Pro Arg Phe Ser Gly Ser
 195 200 205
 Gly Ser Gly Thr Asp Phe Thr Leu Asn Ile His Pro Val Glu Lys Val
 210 215 220
 Asp Ala Ala Thr Tyr His Cys Gln Gln Ser Thr Glu Asp Pro Trp Thr
 225 230 235 240
 Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Ser Gly Gly Gly Gly Ser
 245 250 255
 Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
 260 265 270
 Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr
 275 280 285
 Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
 290 295 300
 Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val
 305 310 315 320

410

Lys Gly Arg Phe Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr
325 330 335

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys
340 345 350

Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
355 360 365

Thr Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly
370 375 380

Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Val Leu Thr Gln Ser
385 390 395 400

Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys
405 410 415

Arg Ala Ser Gln Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro
420 425 430

Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser
435 440 445

Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser
450 455 460

Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys
465 470 475 480

Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
485 490 495

Glu Ile Lys

<210> 382

<211> 1494

<212> DNA

<213> artificial sequence

<220>

<223> CD19xVL2VH5 LHLH

<400> 382
gatatccagc tgaccagtc tccagcttct ttggctgtgt ctctagggca gagggccacc 60
atctcctgca aggccagcca aagtgttgat tatgatggtg atagttattt gaactggtac 120
caacagattc caggacagcc acccaaactc ctcatctatg atgcatccaa tctagtttct 180


```

gggatccac ccaggtttag tggcagtggg tctgggacag acttcaccct caacatccat 240
cctgtggaga aggtggatgc tgcaacctat cactgtcagc aaagtactga ggatccgtgg 300
acgttcggtg gagggaccaa gctcgagatc aaagggtggtg gtggttctgg cggcggcggc 360
tccggtggtg gtggttctca ggtgcagctg cagcagtctg gggctgagct ggtgaggcct 420
gggtcctcag tgaagatttc ctgcaaggct tctggctatg cattcagtag ctactggatg 480
aactgggtga agcagaggcc tggacagggt cttgagtggg ttggacagat ttggcctgga 540
gatggtgata ctaactacaa tggaaagttc aagggtaaag ccactctgac tgcagacgaa 600
tcctccagca cagcctacat gcaactcagc agcctagcat ctgaggactc tgcggtctat 660
ttctgtgcaa gacgggagac tacgacggta ggccggttatt actatgctat ggactactgg 720
ggccaaggga ccacggtcac cgtctcctcc ggagggtggtg gatccgacat tgtactgacc 780
cagtctccag caactctgtc tctgtctcca ggggagcgtg ccaccctgag ctgcagagcc 840
agtcaaagtg taagttacat gaactggtac cagcagaagc cgggcaaggc acccaaaaga 900
tggatttatg acacatccaa agtggcttct ggagtccttg ctgcgttcag tggcagtggg 960
tctgggaccg actactctct cacaatcaac agcttgaggg ctgaagatgc tgccacttat 1020
tactgccaac agtggagtag taaccgctc acgttcggtg gcgggaccaa ggtggagatc 1080
aaaggcgaag gtactagtag tggttctggt ggaagtggag gttcagggtg agcagacgac 1140
gtccaactgg tgcagtcagg ggctgaagtg aaaaaacctg gggcctcagt gaagggtgtcc 1200
tgcaaggctt ctggctacac ctttactagg tacacgatgc actgggtaag gcaggcacct 1260
ggacaggggtc tggaatggat tggatacatt aatcctagcc gtgggttatac taattacgca 1320
gacagcgtca agggccgctt cacaatcact acagacaaat ccaccagcac agcctacatg 1380
gaactgagca gcctgcgttc tgaggacact gcaacctatt actgtgcaag atattatgat 1440
gatcattact gccttgacta ctggggccaa ggcaccacgg tcaccgtctc ctca 1494

```

<210> 383

<211> 498

<212> PRT

<213> artificial sequence

<220>

<223> CD19xVL2VH5 LHLH

<400> 383

```

Asp Ile Gln Leu Thr Gln Ser Pro Ala Ser Leu Ala Val Ser Leu Gly
1           5           10          15

```

```

Gln Arg Ala Thr Ile Ser Cys Lys Ala Ser Gln Ser Val Asp Tyr Asp
                20          25          30

```

Gly Asp Ser Tyr Leu Asn Trp Tyr Gln Gln Ile Pro Gly Gln Pro Pro
 35 40 45

Lys Leu Leu Ile Tyr Asp Ala Ser Asn Leu Val Ser Gly Ile Pro Pro
 50 55 60

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Asn Ile His
 65 70 75 80

Pro Val Glu Lys Val Asp Ala Ala Thr Tyr His Cys Gln Gln Ser Thr
 85 90 95

Glu Asp Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Gly
 100 105 110

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Val
 115 120 125

Gln Leu Gln Gln Ser Gly Ala Glu Leu Val Arg Pro Gly Ser Ser Val
 130 135 140

Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Ser Ser Tyr Trp Met
 145 150 155 160

Asn Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile Gly Gln
 165 170 175

Ile Trp Pro Gly Asp Gly Asp Thr Asn Tyr Asn Gly Lys Phe Lys Gly
 180 185 190

Lys Ala Thr Leu Thr Ala Asp Glu Ser Ser Ser Thr Ala Tyr Met Gln
 195 200 205

Leu Ser Ser Leu Ala Ser Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg
 210 215 220

Arg Glu Thr Thr Thr Val Gly Arg Tyr Tyr Tyr Ala Met Asp Tyr Trp
 225 230 235 240

Gly-Gln-Gly-Thr-Thr-Val-Thr-Val-Ser-Ser-Gly-Gly-Gly-Gly-Ser-Asp
 245 250 255

Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu
 260 265 270

Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Tyr Met Asn
 275 280 285

Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp
 290 295 300

Thr Ser Lys Val Ala Ser Gly Val Pro Ala⁴¹³ Arg Phe Ser Gly Ser Gly
 305 310 315 320
 Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp
 325 330 335
 Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe
 340 345 350
 Gly Gly Gly Thr Lys Val Glu Ile Lys Gly Glu Gly Thr Ser Thr Gly
 355 360 365
 Ser Gly Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Val Gln Leu Val
 370 375 380
 Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val Ser
 385 390 395 400
 Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp Val
 405 410 415
 Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn Pro
 420 425 430
 Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr
 435 440 445
 Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser Ser
 450 455 460
 Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys Ala Arg Tyr Tyr Asp
 465 470 475 480
 Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val
 485 490 495

Ser Ser

<210> 384

<211> 1497

<212> DNA

<213> artificial sequence

<220>

<223> CD19xVL2VH5 HLLH

<400> 384

cagggtgcagc tgcagcagtc tggggctgag ctggtgaggc ctgggtcctc agtgaagatt

414

tcctgcaagg cttctggcta tgcattcagt agctactgga tgaactgggt gaagcagagg	120
cctggacagg gtcttgagtg gattggacag atttggcctg gagatgggtga tactaactac	180
aatggaaagt tcaagggtaa agccactctg actgcagacg aatcctccag cacagcctac	240
atgcaactca gcagcctagc atctgaggac tctgcggtct atttctgtgc aagacgggag	300
actacgacgg taggccgtta ttactatgct atggactact ggggccaagg gaccacggtc	360
accgtctcct ccggtgggtg tggttctggc ggcggcggct ccggtgggtg tggttctgat	420
atccagctga ccaggtctcc agcttctttg gctgtgtctc tagggcagag ggccaccatc	480
tcctgcaagg ccagccaaag tgttgattat gatgggtgata gttatttgaa ctggtaccaa	540
cagattccag gacagccacc caaactcctc atctatgatg catccaatct agtttctggg	600
atcccaccca ggtttagtgg cagtgggtct gggacagact tcaccctcaa catccatcct	660
gtggagaagg tggatgctgc aacctatcac tgtcagcaaa gtactgagga tccgtggacg	720
ttcgggtggag ggaccaagct cgagatcaaa tccggagggtg gtggatccga cattgtactg	780
accagtcctc cagcaactct gtctctgtct ccagggggagc gtgccaccct gagctgcaga	840
gccagtcaaa gtgtaagtta catgaactgg taccagcaga agccgggcaa ggcacccaaa	900
agatggattt atgacacatc caaagtggct tctggagtcc ctgctcgctt cagtggcagt	960
gggtctggga ccgactactc tctcacaatc aacagcttgg aggctgaaga tgctgccact	1020
tattactgcc aacagtggag tagtaacccg ctcacgttcg gtggcgggac caagggtggag	1080
atcaaaggcg aaggtagtag tactggttct ggtggaagtg gaggttcagg tggagcagac	1140
gacgtccaac tgggtgcagtc aggggctgaa gtgaaaaaac ctggggcctc agtgaagggtg	1200
tcctgcaagg cttctggcta cacctttact aggtacacga tgcactgggt aaggcaggca	1260
cctggacagg gtctggaatg gattggatac attaatccta gccgtgggtta tactaattac	1320
gcagacagcg tcaagggccg cttcacaatc actacagaca aatccaccag cacagcctac	1380
atggaactga gcagcctgcg ttctgaggac actgcaacct attactgtgc aagatattat	1440
gatgatcatt actgccttga ctactggggc caaggcacca cggtcaccgt ctctca	1497

<210> 385

<211> 499

<212> PRT

<213> artificial sequence

<220>

<223> CD19xVL2VH5 HLLH

<400> 385

Gln	Val	Gln	Leu	Gln	Gln	Ser	Gly	Ala	Glu	Leu	Val	Arg	Pro	Gly	Ser
1				5				10						15	

ser val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Ser Ser Tyr
 20 25 30 415

Trp Met Asn Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile
 35 40 45

Gly Gln Ile Trp Pro Gly Asp Gly Asp Thr Asn Tyr Asn Gly Lys Phe
 50 55 60

Lys Gly Lys Ala Thr Leu Thr Ala Asp Glu Ser Ser Ser Thr Ala Tyr
 65 70 75 80

Met Gln Leu Ser Ser Leu Ala Ser Glu Asp Ser Ala Val Tyr Phe Cys
 85 90 95

Ala Arg Arg Glu Thr Thr Thr Val Gly Arg Tyr Tyr Tyr Ala Met Asp
 100 105 110

Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly
 115 120 125

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Gln Leu Thr
 130 135 140

Gln Ser Pro Ala Ser Leu Ala Val Ser Leu Gly Gln Arg Ala Thr Ile
 145 150 155 160

Ser Cys Lys Ala Ser Gln Ser Val Asp Tyr Asp Gly Asp Ser Tyr Leu
 165 170 175

Asn Trp Tyr Gln Gln Ile Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr
 180 185 190

Asp Ala Ser Asn Leu Val Ser Gly Ile Pro Pro Arg Phe Ser Gly Ser
 195 200 205

Gly Ser Gly Thr Asp Phe Thr Leu Asn Ile His Pro Val Glu Lys Val
 210 215 220

Asp Ala Ala Thr Tyr His Cys Gln Gln Ser Thr Glu Asp Pro Trp Thr
 225 230 235 240

Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Ser Gly Gly Gly Gly Ser
 245 250 255

Asp Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
 260 265 270

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Tyr Met
 275 280 285

Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr

290 295 416 300
 Asp Thr Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
 305 310 315 320
 Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu
 325 330 335
 Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr
 340 345 350
 Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Gly Glu Gly Thr Ser Thr
 355 360 365
 Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Val Gln Leu
 370 375 380
 Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val
 385 390 395 400
 Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp
 405 410 415
 Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn
 420 425 430
 Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val Lys Gly Arg Phe
 435 440 445
 Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser
 450 455 460
 Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys Ala Arg Tyr Tyr
 465 470 475 480
 Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr
 485 490 495
 Val Ser Ser

<210> 386

<211> 1497

<212> DNA

<213> artificial sequence

<220>

<223> CD19xVH5VL3 HLHL

<400> 386
caggtgcagc tgcagcagtc tggggctgag ctggtgaggg ctgggtcctc agtgaagatt 60
tcctgcaagg cttctggcta tgcattcagt agctactgga tgaactgggt gaagcagagg 120
cctggacagg gtcttgagtg gattggacag atttggcctg gagatgggtga tactaactac 180
aatggaaagt tcaagggtaa agccactctg actgcagacg aatcctccag cacagcctac 240
atgcaactca gcagcctagc atctgaggac tctgcggtct atttctgtgc aagacgggag 300
actacgacgg taggccgcta ttactatgct atggactact ggggccaaagg gaccacggtc 360
accgtctcct ccggtgggtgg tgggttctggc ggcggcggct ccggtgggtgg tgggttctgat 420
atccagctga cccagtctcc agcttctttg gctgtgtctc tagggcagag ggccaccatc 480
tcctgcaagg ccagccaaag tgttgattat gatgggtgata gttatttgaa ctggtaccaa 540
cagattccag gacagccacc caaactcctc atctatgatg catccaatct agtttctggg 600
atcccaccca ggttttagtgg cagtgggtct gggacagact tcaccctcaa catccatcct 660
gtggagaagg tggatgctgc aacctatcac tgtcagcaaa gtactgagga tccgtggacg 720
ttcgggtggag ggaccaagct cgagatcaaa tccggagggtg gtggatccga cgtccaactg 780
gtgcagtcag gggctgaagt gaaaaaacct ggggcctcag tgaagggtgc ctgcaaggct 840
tctggctaca cctttactag gtacacgatg cactgggtaa ggcaggcacc tggacagggt 900
ctggaatgga ttggatacat taatcctagc cgtgggtata ctaattacgc agacagcgtc 960
aagggccgct tcacaatcac tacagacaaa tccaccagca cagcctacat ggaactgagc 1020
agcctgcgtt ctgaggacac tgcaacctat tactgtgcaa gatattatga tgatcattac 1080
tgccttgact actggggcca aggcaccacg gtcaccgtct cctcaggcga aggtactagt 1140
actggttctg gtggaagtgg aggttcaggt ggagcagacg acattgtact gaccagtcct 1200
ccagcaactc tgtctctgtc tccaggggag cgtgccaccc tgacctgcag agccagttca 1260
agtgtaagtt acatgaactg gtaccagcag aagccgggca aggcacccaa aagatggatt 1320
tatgacacat ccaaagtggc ttctggagtc cctgctcgct tcagtggcag tgggtctggg 1380
accgactact ctctcacaat caacagcttg gaggtgaag atgctgccac ttattactgc 1440
caacagtgga gtagtaaccc gctcacgttc ggtggcggga ccaagggtgga gatcaaa 1497

<210> 387

<211> 499

<212> PRT

<213> artificial sequence

<220>

<223> CD19xVH5VL3 HLHL

<400> 387

Gln Val Gln Leu Gln Gln Ser Gly Ala Glu Leu Val Arg Pro Gly Ser

1	5	10	15
ser val Lys	Ile Ser Cys Lys Ala	ser Gly Tyr Ala Phe	ser ser Tyr
	20	25	30
Trp Met Asn	Trp val Lys Gln Arg	Pro Gly Gln Gly	Leu Glu Trp Ile
	35	40	45
Gly Gln Ile	Trp Pro Gly Asp Gly	Asp Thr Asn Tyr	Asn Gly Lys Phe
	50	55	60
Lys Gly Lys	Ala Thr Leu Thr Ala	Asp Glu Ser Ser	Thr Ala Tyr
	65	70	75
Met Gln Leu	Ser Ser Leu Ala Ser	Glu Asp Ser Ala	val Tyr Phe Cys
	85	90	95
Ala Arg Arg	Glu Thr Thr Thr	val Gly Arg Tyr	Tyr Tyr Ala Met Asp
	100	105	110
Tyr Trp Gly	Gln Gly Thr Thr	val Thr val Ser	Ser Gly Gly Gly
	115	120	125
ser Gly Gly	Gly Gly ser Gly Gly	Gly Gly ser Asp	Ile Gln Leu Thr
	130	135	140
Gln ser Pro	Ala Ser Leu Ala	val Ser Leu Gly	Gln Arg Ala Thr Ile
	145	150	155
ser Cys Lys	Ala ser Gln ser	val Asp Tyr Asp	Gly Asp ser Tyr Leu
	165	170	175
Asn Trp Tyr	Gln Gln Ile Pro	Gly Gln Pro Pro	Lys Leu Leu Ile Tyr
	180	185	190
Asp Ala ser	Asn Leu val ser	Gly Ile Pro Pro	Arg Phe ser Gly ser
	195	200	205
Gly ser Gly	Thr Asp Phe Thr	Leu Asn Ile His	Pro val Glu Lys val
	210	215	220
Asp Ala Ala	Thr Tyr His Cys	Gln Gln ser Thr	Glu Asp Pro Trp Thr
	225	230	235
Phe Gly Gly	Gly Thr Lys Leu	Glu Ile Lys ser	Gly Gly Gly Gly ser
	245	250	255
Asp val Gln	Leu val Gln ser	Gly Ala Glu val	Lys Lys Pro Gly Ala
	260	265	270
ser val Lys	val ser Cys Lys	Ala ser Gly Tyr	Thr Phe Thr Arg Tyr
	275	280	285

Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
 290 295 300
 Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val
 305 310 315 320
 Lys Gly Arg Phe Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr
 325 330 335
 Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys
 340 345 350
 Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
 355 360 365
 Thr Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly
 370 375 380
 Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Val Leu Thr Gln Ser
 385 390 395 400
 Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Thr Cys
 405 410 415
 Arg Ala Ser Ser Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro
 420 425 430
 Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser
 435 440 445
 Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser
 450 455 460
 Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys
 465 470 475 480
 Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
 485 490 495
 Glu Ile Lys

<210> 388

<211> 1494

<212> DNA

<213> artificial sequence

<220>

<223> CD19xVL3VH5 LHLH

<400> 388

gatatccagc tgacccagtc tccagcttct ttggctgtgt ctctagggca gagggccacc	60
atctcctgca aggccagcca aagtgttgat tatgatgggtg atagttattt gaactggtac	120
caacagattc caggacagcc acccaaactc ctcatctatg atgcatccaa tctagtttct	180
gggatcccac ccaggtttag tggcagtggg tctgggacag acttcaccct caacatccat	240
cctgtggaga aggtggatgc tgcaacctat cactgtcagc aaagtactga ggatccgtgg	300
acgttcgggtg gagggaccaa gctcgagatc aaaggtgggtg gtggttcttg cggcggcggc	360
tccggtgggtg gtggttctca ggtgcagctg cagcagtctg gggctgagct ggtgaggcct	420
gggtcctcag tgaagatttc ctgcaaggct tctggctatg cattcagtag ctactggatg	480
aactgggtga agcagaggcc tggacagggt cttgagtgga ttggacagat ttggcctgga	540
gatggtgata ctaactacaa tggaaagttc aagggttaaag ccactctgac tgcagacgaa	600
tcctccagca cagcctacat gcaactcagc agcctagcat ctgaggactc tgcggtctat	660
ttctgtgcaa gacgggagac tacgacggta ggccgttatt actatgctat ggactactgg	720
ggccaagggg ccacggtcac cgtctcctcc ggaggtgggtg gatccgacat tgtactgacc	780
cagtctccag caactctgtc tctgtctcca ggggagcgtg ccaccctgac ctgcagagcc	840
agttcaagtg taagttacat gaactggtac cagcagaagc cgggcaaggc acccaaaaga	900
tggatttatg acacatccaa agtggcttct ggagtccctg ctgccttcag tggcagtggg	960
tctgggaccg actactctct cacaatcaac agcttggagg ctgaagatgc tgccacttat	1020
tactgccaac agtggagtag taaccgctc acgttcgggtg gcgggaccaa ggtggagatc	1080
aaaggcgaag gtactagtag tggttctggt ggaagtggag gttcagggtgg agcagacgac	1140
gtccaactgg tgcagtcagg ggctgaagtg aaaaaacctg gggcctcagt gaagggtgtcc	1200
tgcaaggctt ctggctacac ctttactagg tacacgatgc actgggtaag gcaggcacct	1260
ggacagggtc tggaatggat tggatacatt aatcctagcc gtggttatac taattacgca	1320
gacagcgtca agggccgctt cacaatcact acagacaaat ccaccagcac agcctacatg	1380
gaactgagca gcctgcgttc tgaggacact gcaacctatt actgtgcaag atattatgat	1440
gatcattact gccttgacta ctggggccaa ggcaccacgg tcaccgtctc ctca	1494

<210> 389

<211> 498

<212> PRT

<213> artificial sequence

<220>

<223> CD19xVL3VH5 LHLH

<400> 389

Asp Ile Gln Leu Thr Gln Ser Pro Ala Ser Leu Ala Val Ser Leu Gly
 1 5 10 15
 Gln Arg Ala Thr Ile Ser Cys Lys Ala Ser Gln Ser Val Asp Tyr Asp
 20 25 30
 Gly Asp Ser Tyr Leu Asn Trp Tyr Gln Gln Ile Pro Gly Gln Pro Pro
 35 40 45
 Lys Leu Leu Ile Tyr Asp Ala Ser Asn Leu Val Ser Gly Ile Pro Pro
 50 55 60
 Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Asn Ile His
 65 70 75 80
 Pro Val Glu Lys Val Asp Ala Ala Thr Tyr His Cys Gln Gln Ser Thr
 85 90 95
 Glu Asp Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Gly
 100 105 110
 Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Val
 115 120 125
 Gln Leu Gln Gln Ser Gly Ala Glu Leu Val Arg Pro Gly Ser Ser Val
 130 135 140
 Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Ser Ser Tyr Trp Met
 145 150 155 160
 Asn Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile Gly Gln
 165 170 175
 Ile Trp Pro Gly Asp Gly Asp Thr Asn Tyr Asn Gly Lys Phe Lys Gly
 180 185 190
 Lys Ala Thr Leu Thr Ala Asp Glu Ser Ser Ser Thr Ala Tyr Met Gln
 195 200 205
 Leu Ser Ser Leu Ala Ser Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg
 210 215 220
 Arg Glu Thr Thr Thr Val Gly Arg Tyr Tyr Tyr Ala Met Asp Tyr Trp
 225 230 235 240
 Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp
 245 250 255
 Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu
 260 265 270

Arg Ala Thr Leu Thr Cys Arg Ala Ser Ser Ser Val Ser Tyr Met Asn
 275 280 285

Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp
 290 295 300

Thr Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser Gly
 305 310 315 320

Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp
 325 330 335

Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe
 340 345 350

Gly Gly Gly Thr Lys Val Glu Ile Lys Gly Glu Gly Thr Ser Thr Gly
 355 360 365

Ser Gly Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Val Gln Leu Val
 370 375 380

Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val Ser
 385 390 395 400

Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp Val
 405 410 415

Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn Pro
 420 425 430

Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr
 435 440 445

Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser Ser
 450 455 460

Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys Ala Arg Tyr Tyr Asp
 465 470 475 480

Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val
 485 490 495

Ser Ser

<210> 390

<211> 1497

<212> DNA

<213> artificial sequence

<220>

<223> CD19xVL3VH5 HLLH

<400> 390

caggtgcagc tgcagcagtc tggggctgag ctggtgaggc ctgggtcctc agtgaagatt	60
tcctgcaagg cttctggcta tgcattcagt agctactgga tgaactgggt gaagcagagg	120
cctggacagg gtcttgagtg gattggacag atttggcctg gagatgggtga tactaactac	180
aatggaaagt tcaagggtaa agccactctg actgcagacg aatcctccag cacagcctac	240
atgcaactca gcagcctagc atctgaggac tctgcggtct atttctgtgc aagacgggag	300
actacgacgg taggccgtta ttactatgct atggactact ggggccaagg gaccacggtc	360
accgtctcct ccggtgggtgg tggttctggc ggcggcggct ccggtgggtgg tggttctgat	420
atccagctga cccagtctcc agcttctttg gctgtgtctc tagggcagag ggccaccatc	480
tcctgcaagg ccagccaaag tggtgattat gatggtgata gttatttgaa ctggtaccaa	540
cagattccag gacagccacc caaactcctc atctatgatg catccaatct agtttctggg	600
atcccacca ggtttagtgg cagtgggtct gggacagact tcaccctcaa catccatcct	660
gtggagaagg tggatgctgc aacctatcac tgtcagcaaa gtactgagga tccgtggacg	720
ttcgggtggag ggaccaagct cgagatcaaa tccggagggtg gtggatccga cattgtactg	780
accagtctc cagcaactct gtctctgtct ccaggggagc gtgccaccct gacctgcaga	840
gccagttcaa gtgtaagtta catgaactgg taccagcaga agccgggcaa ggcacccaaa	900
agatggattt atgacacatc caaagtggct tctggagtcc ctgctcgctt cagtggcagt	960
gggtctggga ccgactactc tctcacaatc aacagcttgg aggctgaaga tgctgccact	1020
tattactgcc aacagtggag tagtaacccg ctcacgttcg gtggcgggac caaggtggag	1080
atcaaaggcg aaggtactag tactggttct ggtggaagtg gaggttcagg tggagcagac	1140
gacgtccaac tgggtgcagtc aggggctgaa gtgaaaaaac ctggggcctc agtgaagggtg	1200
tcctgcaagg cttctggcta cacctttact aggtacacga tgcactgggt aaggcaggca	1260
cctggacagg gtctggaatg gattggatac attaatccta gccgtgggtta tactaattac	1320
gcagacagcg tcaagggccg cttcacaatc actacagaca aatccaccag cacagcctac	1380
atggaactga gcagcctgcg ttctgaggac actgcaacct attactgtgc aagatattat	1440
gatgatcatt actgccttga ctactggggc caaggcacca cggtcaccgt ctctca	1497

<210> 391

<211> 499

<212> PRT

<213> artificial sequence

<220>

<223> CD19xVL3VH5 HLLH

<400> 391

Gln Val Gln Leu Gln Gln Ser Gly Ala Glu Leu Val Arg Pro Gly Ser
 1 5 10 15

Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Ser Ser Tyr
 20 25 30

Trp Met Asn Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile
 35 40 45

Gly Gln Ile Trp Pro Gly Asp Gly Asp Thr Asn Tyr Asn Gly Lys Phe
 50 55 60

Lys Gly Lys Ala Thr Leu Thr Ala Asp Glu Ser Ser Ser Thr Ala Tyr
 65 70 75 80

Met Gln Leu Ser Ser Leu Ala Ser Glu Asp Ser Ala Val Tyr Phe Cys
 85 90 95

Ala Arg Arg Glu Thr Thr Thr Val Gly Arg Tyr Tyr Tyr Ala Met Asp
 100 105 110

Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly
 115 120 125

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Gln Leu Thr
 130 135 140

Gln Ser Pro Ala Ser Leu Ala Val Ser Leu Gly Gln Arg Ala Thr Ile
 145 150 155 160

Ser Cys Lys Ala Ser Gln Ser Val Asp Tyr Asp Gly Asp Ser Tyr Leu
 165 170 175

Asn Trp Tyr Gln Gln Ile Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr
 180 185 190

Asp Ala Ser Asn Leu Val Ser Gly Ile Pro Pro Arg Phe Ser Gly Ser
 195 200 205

Gly Ser Gly Thr Asp Phe Thr Leu Asn Ile His Pro Val Glu Lys Val
 210 215 220

Asp Ala Ala Thr Tyr His Cys Gln Gln Ser Thr Glu Asp Pro Trp Thr
 225 230 235 240

Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Ser Gly Gly Gly Gly Ser
 245 250 255

Asp Ile Val Leu Thr Gln Ser Pro Ala Thr⁴²⁵ Leu Ser Leu Ser Pro Gly
260 265 270

Glu Arg Ala Thr Leu Thr Cys Arg Ala Ser Ser Ser Val Ser Tyr Met
275 280 285

Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr
290 295 300

Asp Thr Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
305 310 315 320

Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu
325 330 335

Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr
340 345 350

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Gly Glu Gly Thr Ser Thr
355 360 365

Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Val Gln Leu
370 375 380

Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val
385 390 395 400

Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp
405 410 415

Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn
420 425 430

Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val Lys Gly Arg Phe
435 440 445

Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser
450 455 460

Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys Ala Arg Tyr Tyr
465 470 475 480

Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr
485 490 495

Val Ser Ser

<210> 392

<211> 1497

<212> DNA

<213> artificial sequence

<220>

<223> CD19xVH7VL1 HLHL

<400> 392

caggtgcagc tgcagcagtc tggggctgag ctggtgaggc ctgggtcctc agtgaagatt	60
tcctgcaagg cttctggcta tgcattcagt agctactgga tgaactgggt gaagcagagg	120
cctggacagg gtcttgagtg gattggacag atttggcctg gagatgggtga tactaactac	180
aatggaaagt tcaagggtaa agccactctg actgcagacg aatcctccag cacagcctac	240
atgcaactca gcagcctagc atctgaggac tctgcggtct atttctgtgc aagacgggag	300
actacgacgg taggccgtta ttactatgct atggactact ggggccaagg gaccacggtc	360
accgtctcct ccggtggtgg tggttctggc ggcggcggct ccggtggtgg tggttctgat	420
atccagctga ccagctctcc agcttctttg gctgtgtctc tagggcagag ggccaccatc	480
tcctgcaagg ccagccaaag tgttgattat gatggtgata gttatttgaa ctggtaccaa	540
cagattccag gacagccacc caaactcctc atctatgatg catccaatct agtttctggg	600
atcccaccca ggtttagtgg cagtgggtct gggacagact tcaccctcaa catccatcct	660
gtggagaagg tggatgctgc aacctatcac tgtcagcaaa gtactgagga tccgtggacg	720
ttcgggtggag ggaccaagct cgagatcaaa tccggagggtg gtggatccga cgtccaactg	780
gtgcagtcag gggctgaagt gaaaaaacct ggggcctcag tgaagggtgtc ctgcaaggct	840
tctggctaca cttttactag gtacacgatg cactgggtaa ggcaggcacc tggacagggt	900
ctggaatgga ttggatacat taatcctagc cgtgggttata ctaattacaa tcagaagttc	960
aaggaccgcg tcacaatcac tacagacaaa tccaccagca cagcctacat ggaactgagc	1020
agcctgcgtt ctgaggacac tgcagtctat tactgtgcaa gatattatga tgatcattac	1080
tgccttgact actggggcca aggcaccacg gtcaccgtct cctcaggcga aggtactagt	1140
actggttctg gtggaagtgg aggttcaggt ggagcagacg acattcagat gaccagttct	1200
ccatctagcc tgtctgcatc tgtcggggac cgtgtcacca tcacctgcag agccagtcaa	1260
agtgtaagtt acatgaactg gtaccagcag aagccgggca aggcacccaa aagatggatt	1320
tatgacacat ccaaagtggc ttctggagtc cctgctcgct tcagtggcag tgggtctggg	1380
accgactact ctctcacaat caacagcttg gaggtgaag atgctgccac ttattactgc	1440
caacagtgga gtagtaacct gtcacgttc ggtggcggga ccaagggtgga gatcaaa	1497

<210> 393

<211> 499

<212> PRT

<213> artificial sequence

<220>

<223> CD19xVH7VL1 HLHL

<400> 393

Gln Val Gln Leu Gln Gln Ser Gly Ala Glu Leu Val Arg Pro Gly Ser
1 5 10 15

Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Ser Ser Tyr
20 25 30

Trp Met Asn Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Gln Ile Trp Pro Gly Asp Gly Asp Thr Asn Tyr Asn Gly Lys Phe
50 55 60

Lys Gly Lys Ala Thr Leu Thr Ala Asp Glu Ser Ser Ser Thr Ala Tyr
65 70 75 80

Met Gln Leu Ser Ser Leu Ala Ser Glu Asp Ser Ala Val Tyr Phe Cys
85 90 95

Ala Arg Arg Glu Thr Thr Thr Val Gly Arg Tyr Tyr Tyr Ala Met Asp
100 105 110

Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly
115 120 125

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Gln Leu Thr
130 135 140

Gln Ser Pro Ala Ser Leu Ala Val Ser Leu Gly Gln Arg Ala Thr Ile
145 150 155 160

Ser Cys Lys Ala Ser Gln Ser Val Asp Tyr Asp Gly Asp Ser Tyr Leu
165 170 175

Asn Trp Tyr Gln Gln Ile Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr
180 185 190

Asp Ala Ser Asn Leu Val Ser Gly Ile Pro Pro Arg Phe Ser Gly Ser
195 200 205

Gly Ser Gly Thr Asp Phe Thr Leu Asn Ile His Pro Val Glu Lys Val
210 215 220

Asp Ala Ala Thr Tyr His Cys Gln Gln Ser Thr Glu Asp Pro Trp Thr
225 230 235 240

Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Ser Gly Gly Gly Gly Ser

<211> 1494

<212> DNA

<213> artificial sequence

<220>

<223> CD19xVL1VH7 LHLH

<400> 394

gatatccagc	tgacccagtc	tccagcttct	ttggctgtgt	ctctagggca	gagggccacc	60
atctcctgca	aggccagcca	aagtgttgat	tatgatggtg	atagttat	gaactggtac	120
caacagattc	caggacagcc	acccaaactc	ctcatctatg	atgcatccaa	tctagtttct	180
gggatcccac	ccaggtttag	tggcagtggg	tctgggacag	acttcaccct	caacatccat	240
cctgtggaga	aggtggatgc	tgcaacctat	cactgtcagc	aaagtactga	ggatccgtgg	300
acgttcggtg	gagggaccaa	gctcgagatc	aaagggtggtg	gtggttctgg	cggcggcggc	360
tccggtggtg	gtggttctca	ggtgcagctg	cagcagtctg	gggctgagct	ggtgaggcct	420
gggtcctcag	tgaagatttc	ctgcaaggct	tctggctatg	cattcagtag	ctactggatg	480
aactgggtga	agcagaggcc	tggacagggt	cttgagtgga	ttggacagat	ttggcctgga	540
gatggtgata	ctaactacaa	tggaaagtgc	aagggtaaag	ccactctgac	tgcagacgaa	600
tcctccagca	cagcctacat	gcaactcagc	agcctagcat	ctgaggactc	tgcggtctat	660
ttctgtgcaa	gacgggagac	tacgacggtg	ggccgttatt	actatgctat	ggactactgg	720
ggccaaggga	ccacggtcac	cgtctcctcc	ggagggtggtg	gatccgacat	tcagatgacc	780
cagtctccat	ctagcctgtc	tgcattctgtc	ggggaccgtg	tcaccatcac	ctgcagagcc	840
agtcaaagtg	taagttacat	gaactggtac	cagcagaagc	cgggcaaggc	acccaaaaga	900
tggatttatg	acacatccaa	agtggcttct	ggagtccttg	ctcgcttcag	tggcagtggg	960
tctgggaccg	actactctct	cacaatcaac	agcttgaggg	ctgaagatgc	tgccacttat	1020
tactgccaac	agtggagtag	taacccgctc	acgttcggtg	gcgggaccaa	ggtggagatc	1080
aaaggcgaag	gtactagtag	tgggttctgg	ggaagtggag	gttcagggtg	agcagacgac	1140
gtccaactgg	tgcagtcagg	ggctgaagtg	aaaaaacctg	gggcctcagt	gaagggtgtcc	1200
tgcaaggctt	ctggctacac	ctttactagg	tacacgatgc	actgggtaag	gcaggcacct	1260
ggacagggtc	tggaatggat	tggatacatt	aatcctagcc	gtgggttatac	taattacaat	1320
cagaagttca	aggaccgcgt	cacaatcact	acagacaaat	ccaccagcac	agcctacatg	1380
gaactgagca	gcctgcgttc	tgaggacact	gcagtctatt	actgtgcaag	atattatgat	1440
gatcattact	gccttgacta	ctggggccaa	ggcaccacgg	tcaccgtctc	ctca	1494

<210> 395

<211> 498

<212> PRT

<213> artificial sequence

<220>

<223> CD19xVL1VH7 LHLH

<400> 395

Asp Ile Gln Leu Thr Gln Ser Pro Ala Ser Leu Ala Val Ser Leu Gly
1 5 10 15

Gln Arg Ala Thr Ile Ser Cys Lys Ala Ser Gln Ser Val Asp Tyr Asp
20 25 30

Gly Asp Ser Tyr Leu Asn Trp Tyr Gln Gln Ile Pro Gly Gln Pro Pro
35 40 45

Lys Leu Leu Ile Tyr Asp Ala Ser Asn Leu Val Ser Gly Ile Pro Pro
50 55 60

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Asn Ile His
65 70 75 80

Pro Val Glu Lys Val Asp Ala Ala Thr Tyr His Cys Gln Gln Ser Thr
85 90 95

Glu Asp Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Gly
100 105 110

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Val
115 120 125

Gln Leu Gln Gln Ser Gly Ala Glu Leu Val Arg Pro Gly Ser Ser Val
130 135 140

Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Ser Ser Tyr Trp Met
145 150 155 160

Asn Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile Gly Gln
165 170 175

Ile Trp Pro Gly Asp Gly Asp Thr Asn Tyr Asn Gly Lys Phe Lys Gly
180 185 190

Lys Ala Thr Leu Thr Ala Asp Glu Ser Ser Ser Thr Ala Tyr Met Gln
195 200 205

Leu Ser Ser Leu Ala Ser Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg
210 215 220

Arg Glu Thr Thr Thr Val Gly Arg Tyr Tyr Tyr Ala Met Asp Tyr Trp
225 230 235 240

Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp
 245 250 255
 Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp
 260 265 270
 Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Ser Tyr Met Asn
 275 280 285
 Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp
 290 295 300
 Thr Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser Gly
 305 310 315 320
 Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp
 325 330 335
 Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe
 340 345 350
 Gly Gly Gly Thr Lys Val Glu Ile Lys Gly Glu Gly Thr Ser Thr Gly
 355 360 365
 Ser Gly Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Val Gln Leu Val
 370 375 380
 Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val Ser
 385 390 395 400
 Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp Val
 405 410 415
 Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn Pro
 420 425 430
 Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe Lys Asp Arg Val Thr
 435 440 445
 Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser Ser
 450 455 460
 Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Tyr Tyr Asp
 465 470 475 480
 Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val
 485 490 495
 Ser Ser

<210> 396
 <211> 1497
 <212> DNA
 <213> artificial sequence

<220>

<223> CD19xVL1VH7 HLLH

<400> 396
 caggtgcagc tgcagcagtc tggggctgag ctggtgaggc ctgggtcctc agtgaagatt 60
 tcctgcaagg cttctggcta tgcattcagt agctactgga tgaactgggt gaagcagagg 120
 cctggacagg gtcttgagtg gattggacag atttggcctg gagatgggtga tactaactac 180
 aatggaaagt tcaagggtaa agccactctg actgcagacg aatcctccag cacagcctac 240
 atgcaactca gcagcctagc atctgaggac tctgcggtct atttctgtgc aagacgggag 300
 actacgacgg taggccgtta ttactatgct atggactact ggggccaagg gaccacggtc 360
 accgtctcct ccggtgggtg tggttctggc ggcggcggct ccggtgggtg tggttctgat 420
 atccagctga ccagctctcc agcttctttg gctgtgtctc tagggcagag ggccaccatc 480
 tcctgcaagg ccagccaaag tgttgattat gatggtgata gttatttgaa ctggtaccaa 540
 cagattccag gacagccacc caaactcctc atctatgatg catccaatct agtttctggg 600
 atcccaccca ggtttagtggt cagtgggtct gggacagact tcaccctcaa catccatcct 660
 gtggagaagg tggatgctgc aacctatcac tgtcagcaaa gtactgagga tccgtggacg 720
 ttcggtggag ggaccaagct cgagatcaaa tccggagggtg gtggatccga cattcagatg 780
 acccagtctc catctagcct gtctgcatct gtcggggacc gtgtcaccat cacctgcaga 840
 gccagtcaaa gtgtaagtta catgaactgg taccagcaga agccgggcaa ggcacccaaa 900
 agatggattt atgacacatc caaagtggct tctggagtcc ctgctcgctt cagtggcagt 960
 ggggtctggga ccgactactc tctcacaatc aacagcttgg aggctgaaga tgctgccact 1020
 tattactgcc aacagtggag tagtaacccg ctcacgttcg gtggcgggac caaggtggag 1080
 atcaaaggcg aaggtactag tactggttct ggtggaagtg gaggttcagg tggagcagac 1140
 gacgtccaac tgggtgcagtc aggggctgaa gtgaaaaaac ctggggcctc agtgaagggtg 1200
 tcctgcaagg cttctggcta cacctttact aggtacacga tgcactgggt aaggcaggca 1260
 cctggacagg gtctggaatg gattggatac attaaticcta gccgtgggtta tactaattac 1320
 aatcagaagt tcaaggaccg cgtcacaatc actacagaca aatccaccag cacagcctac 1380
 atggaactga gcagcctgcg ttctgaggac actgcagtct attactgtgc aagatattat 1440
 gatgatcatt actgccttga ctactggggc caaggcacca cggtcaccgt ctcctca 1497

<210> 397

<211> 499

<212> PRT

<213> artificial sequence

<220>

<223> CD19xVL1VH7 HLLH

<400> 397

Gln Val Gln Leu Gln Gln Ser Gly Ala Glu Leu Val Arg Pro Gly Ser
 1 5 10 15

Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Ser Ser Tyr
 20 25 30

Trp Met Asn Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile
 35 40 45

Gly Gln Ile Trp Pro Gly Asp Gly Asp Thr Asn Tyr Asn Gly Lys Phe
 50 55 60

Lys Gly Lys Ala Thr Leu Thr Ala Asp Glu Ser Ser Ser Thr Ala Tyr
 65 70 75 80

Met Gln Leu Ser Ser Leu Ala Ser Glu Asp Ser Ala Val Tyr Phe Cys
 85 90 95

Ala Arg Arg Glu Thr Thr Thr Val Gly Arg Tyr Tyr Tyr Ala Met Asp
 100 105 110

Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly
 115 120 125

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Gln Leu Thr
 130 135 140

Gln Ser Pro Ala Ser Leu Ala Val Ser Leu Gly Gln Arg Ala Thr Ile
 145 150 155 160

Ser Cys Lys Ala Ser Gln Ser Val Asp Tyr Asp Gly Asp Ser Tyr Leu
 165 170 175

Asn Trp Tyr Gln Gln Ile Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr
 180 185 190

Asp Ala Ser Asn Leu Val Ser Gly Ile Pro Pro Arg Phe Ser Gly Ser
 195 200 205

Gly Ser Gly Thr Asp Phe Thr Leu Asn Ile His Pro Val Glu Lys Val
 210 215 220

Asp Ala Ala Thr Tyr His Cys Gln Gln Ser Thr Glu Asp Pro Trp Thr
225 230 235 240

Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Ser Gly Gly Gly Gly Ser
245 250 255

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
260 265 270

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Ser Tyr Met
275 280 285

Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr
290 295 300

Asp Thr Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
305 310 315 320

Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu
325 330 335

Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr
340 345 350

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Gly Glu Gly Thr Ser Thr
355 360 365

Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Val Gln Leu
370 375 380

Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val
385 390 395 400

Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp
405 410 415

Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn
420 425 430

~~Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe Lys Asp Arg Val~~
435 440 445

Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser
450 455 460

Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Tyr Tyr
465 470 475 480

Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr
485 490 495

val ser ser

<210> 398

<211> 1497

<212> DNA

<213> artificial sequence

<220>

<223> CD19xVH7VL2 HLHL

<400> 398

caggtgcagc tgcagcagtc tggggctgag ctggtgaggc ctgggtcctc agtgaagatt	60
tcctgcaagg cttctggcta tgcattcagt agctactgga tgaactgggt gaagcagagg	120
cctggacagg gtcttgagtg gattggacag atttggcctg gagatgggtga tactaactac	180
aatggaaagt tcaagggtaa agccactctg actgcagacg aatcctccag cacagcctac	240
atgcaactca gcagcctagc atctgaggac tctgcggtct atttctgtgc aagacgggag	300
actacgacgg taggccgtta ttactatgct atggactact ggggcccaagg gaccacggtc	360
accgtctcct ccggtgggtgg tggttctggc ggcggcggct ccggtgggtgg tggttctgat	420
atccagctga ccagtcctcc agcttctttg gctgtgtctc tagggcagag ggccaccatc	480
tcctgcaagg ccagccaaag tggtgattat gatggtgata gttatttgaa ctggtaccaa	540
cagattccag gacagccacc caaactcctc atctatgatg catccaatct agtttctggg	600
atcccaccca ggtttagtgg cagtgggtct gggacagact tcaccctcaa catccatcct	660
gtggagaagg tggatgctgc aacctatcac tgtcagcaaa gtactgagga tccgtggacg	720
ttcgggtggag ggaccaagct cgagatcaaa tccggaggtg gtggatccga cgtccaactg	780
gtgcagtcag gggctgaagt gaaaaaacct ggggcctcag tgaaggtgtc ctgcaaggct	840
tctggctaca cttttactag gtacacgatg cactgggtaa ggcaggcacc tggacagggt	900
ctggaatgga ttggatacat taatcctagc cgtgggttata ctaattacaa tcagaagtgc	960
aaggaccgcg tcacaatcac tacagacaaa tccaccagca cagcctacat ggaactgagc	1020
agcctgcgtt ctgaggacac tgcagtctat tactgtgcaa gatattatga tgatcattac	1080
tgccttgact actggggcca aggcaccacg gtcaccgtct cctcaggcga aggtactagt	1140
actggttctg gtggaagtgg aggttcaggt ggagcagacg acattgtact gaccagtcct	1200
ccagcaactc tgtctctgtc tccaggggag cgtgccaccc tgagctgcag agccagtcaa	1260
agtgtaagtt acatgaactg gtaccagcag aagccgggca aggcacccaa aagatggatt	1320
tatgacacat ccaaagtggc ttctggagtc cctgctcgct tcagtggcag tgggtctggg	1380
accgactact ctctcacaat caacagcttg gaggctgaag atgctgccac ttattactgc	1440
caacagtgga gtagtaaccc gctcacgttc ggtggcggga ccaaggtgga gatcaaa	1497

<210> 399

<211> 499

<212> PRT

<213> artificial sequence

<220>

<223> CD19xVH7VL2 HLHL

<400> 399

Gln Val Gln Leu Gln Gln Ser Gly Ala Glu Leu Val Arg Pro Gly Ser
1 5 10 15

Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Ser Ser Tyr
20 25 30

Trp Met Asn Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Gln Ile Trp Pro Gly Asp Gly Asp Thr Asn Tyr Asn Gly Lys Phe
50 55 60

Lys Gly Lys Ala Thr Leu Thr Ala Asp Glu Ser Ser Ser Thr Ala Tyr
65 70 75 80

Met Gln Leu Ser Ser Leu Ala Ser Glu Asp Ser Ala Val Tyr Phe Cys
85 90 95

Ala Arg Arg Glu Thr Thr Thr Val Gly Arg Tyr Tyr Tyr Ala Met Asp
100 105 110

Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly
115 120 125

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Gln Leu Thr
130 135 140

Gln Ser Pro Ala Ser Leu Ala Val Ser Leu Gly Gln Arg Ala Thr Ile
145 150 155 160

Ser Cys Lys Ala Ser Gln Ser Val Asp Tyr Asp Gly Asp Ser Tyr Leu
165 170 175

Asn Trp Tyr Gln Gln Ile Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr
180 185 190

Asp Ala Ser Asn Leu Val Ser Gly Ile Pro Pro Arg Phe Ser Gly Ser
195 200 205

Gly Ser Gly Thr Asp Phe Thr⁴³⁷ Leu Asn Ile His Pro Val Glu Lys Val
 210 215 220

Asp Ala Ala Thr Tyr His Cys Gln Gln Ser Thr Glu Asp Pro Trp Thr
 225 230 235 240

Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Ser Gly Gly Gly Gly Ser
 245 250 255

Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
 260 265 270

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr
 275 280 285

Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
 290 295 300

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe
 305 310 315 320

Lys Asp Arg Val Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr
 325 330 335

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
 340 345 350

Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
 355 360 365

Thr Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly
 370 375 380

Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Val Leu Thr Gln Ser
 385 390 395 400

Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys
 405 410 415

Arg Ala Ser Gln Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro
 420 425 430

Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser
 435 440 445

Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser
 450 455 460

Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys
 465 470 475 480

Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val

485

438
490

495

Glu Ile Lys

<210> 400

<211> 1494

<212> DNA

<213> artificial sequence

<220>

<223> CD19xVL2VH7 LHLH

<400> 400

gatatccagc	tgacccagtc	tccagcttct	ttggctgtgt	ctctagggca	gagggccacc	60
atctcctgca	aggccagcca	aagtgttgat	tatgatggtg	atagttat	gaactggtac	120
caacagattc	caggacagcc	acccaaactc	ctcatctatg	atgcatccaa	tctagtttct	180
gggatcccac	ccaggtttag	tggcagtggg	tctgggacag	acttcaccct	caacatccat	240
cctgtggaga	aggtggatgc	tgcaacctat	cactgtcagc	aaagtactga	ggatccgtgg	300
acgttcggtg	gagggaccaa	gctcgagatc	aaaggtggtg	gtggttctgg	cggcggcggc	360
tccggtggtg	gtggttctca	ggtgcagctg	cagcagtctg	gggctgagct	ggtgaggcct	420
gggtcctcag	tgaagatttc	ctgcaaggct	tctggctatg	cattcagtag	ctactggatg	480
aactgggtga	agcagaggcc	tggacagggt	cttgagtgga	ttggacagat	ttggcctgga	540
gatggtgata	ctaactacaa	tggaaagttc	aagggtaaag	ccactctgac	tgacagacgaa	600
tcctccagca	cagcctacat	gcaactcagc	agcctagcat	ctgaggactc	tgccgtctat	660
ttctgtgcaa	gacgggagac	tacgacggta	ggccgttatt	actatgctat	ggactactgg	720
ggccaaggga	ccacggtcac	cgtctcctcc	ggaggtggtg	gatccgacat	tgtactgacc	780
cagtctccag	caactctgtc	tctgtctcca	ggggagcgtg	ccaccctgag	ctgcagagcc	840
agtcaaagtg	taagttacat	gaactggtac	cagcagaagc	cgggcaaggc	acccaaaaga	900
tggatttatg	acacatccaa	agtggcttct	ggagtccctg	ctcgcttcag	tggcagtggg	960
tctgggaccg	actactctct	cacaatcaac	agcttgaggg	ctgaagatgc	tgccacttat	1020
tactgccaac	agtggagtag	taacccgctc	acgttcggtg	gcgggaccaa	ggtggagatc	1080
aaaggcgaag	gtactagtag	tggttctggt	ggaagtggag	gttcagggtg	agcagacgac	1140
gtccaactgg	tgacgtcagg	ggctgaagtg	aaaaaacctg	gggcctcagt	gaaggtgtcc	1200
tgcaaggctt	ctggctacac	ctttactagg	tacacgatgc	actgggtaag	gcaggcacct	1260
ggacagggtc	tggaatggat	tggatacatt	aatcctagcc	gtggttatac	taattacaat	1320
cagaagttca	aggaccgcgt	cacaatcact	acagacaaat	ccaccagcac	agcctacatg	1380
gaactgagca	gcctgcgttc	tgaggacact	gcagtctatt	actgtgcaag	atattatgat	1440

gatcattact gccttgacta ctggggccaa ggcaccacgg tcaccgtctc ctca

1494

<210> 401

<211> 498

<212> PRT

<213> artificial sequence

<220>

<223> CD19xVL2VH7 LHLH

<400> 401

Asp Ile Gln Leu Thr Gln Ser Pro Ala Ser Leu Ala Val Ser Leu Gly
1 5 10 15

Gln Arg Ala Thr Ile Ser Cys Lys Ala Ser Gln Ser Val Asp Tyr Asp
20 25 30

Gly Asp Ser Tyr Leu Asn Trp Tyr Gln Gln Ile Pro Gly Gln Pro Pro
35 40 45

Lys Leu Leu Ile Tyr Asp Ala Ser Asn Leu Val Ser Gly Ile Pro Pro
50 55 60

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Asn Ile His
65 70 75 80

Pro Val Glu Lys Val Asp Ala Ala Thr Tyr His Cys Gln Gln Ser Thr
85 90 95

Glu Asp Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Gly
100 105 110

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Val
115 120 125

Gln Leu Gln Gln Ser Gly Ala Glu Leu Val Arg Pro Gly Ser Ser Val
130 135 140

Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Ser Ser Tyr Trp Met
145 150 155 160

Asn Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile Gly Gln
165 170 175

Ile Trp Pro Gly Asp Gly Asp Thr Asn Tyr Asn Gly Lys Phe Lys Gly
180 185 190

Lys Ala Thr Leu Thr Ala Asp Glu Ser Ser Ser Thr Ala Tyr Met Gln

195	200	440	205
Leu 210	Ser Ser Leu Ala Ser 215	Glu Asp Ser Ala Val 220	Tyr Phe Cys Ala Arg
Arg 225	Glu Thr Thr Thr Val 230	Gly Arg Tyr Tyr 235	Ala Met Asp Tyr Trp 240
Gly Gln Gly Thr 245	Thr Val Ser 250	Gly Gly Gly Gly 255	Ser Asp
Ile Val Leu 260	Thr Gln Ser Pro Ala 265	Thr Leu Ser Leu Ser 270	Pro Gly Glu
Arg Ala 275	Thr Leu Ser Cys Arg 280	Ala Ser Gln Ser Val 285	Ser Tyr Met Asn
Trp 290	Tyr Gln Gln Lys Pro 295	Gly Lys Ala Pro Lys 300	Arg Trp Ile Tyr Asp
Thr 305	Ser Lys Val Ala 310	Ser Gly Val Pro Ala 315	Arg Phe Ser Gly Ser Gly 320
Ser Gly Thr Asp 325	Tyr Ser Leu Thr Ile 330	Asn Ser Leu Glu Ala 335	Glu Asp
Ala Ala Thr 340	Tyr Tyr Cys Gln Gln 345	Trp Ser Ser Asn Pro 350	Leu Thr Phe
Gly Gly Gly 355	Thr Lys Val Glu 360	Ile Lys Gly Glu Gly 365	Thr Ser Thr Gly
Ser 370	Gly Gly Ser Gly Gly 375	Ser Gly Gly Ala Asp 380	Asp Val Gln Leu Val
Gln 385	Ser Gly Ala Glu 390	Val Lys Lys Pro Gly 395	Ala Ser Val Lys Val Ser 400
Cys Lys Ala Ser 405	Gly Tyr Thr Phe Thr 410	Arg Tyr Thr Met His 415	Trp Val
Arg Gln Ala 420	Pro Gly Gln Gly Leu 425	Glu Trp Ile Gly Tyr 430	Ile Asn Pro
Ser Arg 435	Gly Tyr Thr Asn Tyr 440	Asn Gln Lys Phe Lys 445	Asp Arg Val Thr
Ile 450	Thr Thr Asp Lys Ser 455	Thr Ser Thr Ala Tyr 460	Met Glu Leu Ser Ser
Leu 465	Arg Ser Glu Asp 470	Thr Ala Val Tyr Tyr 475	Cys Ala Arg Tyr Tyr Asp 480

Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val
 485 490 495

Ser Ser

<210> 402

<211> 1497

<212> DNA

<213> artificial sequence

<220>

<223> CD19xVL2VH7 HLLH

<400> 402

caggtgcagc tgcagcagtc tggggctgag ctggtgaggc ctgggtcctc agtgaagatt	60
tcctgcaagg cttctggcta tgcattcagt agctactgga tgaactgggt gaagcagagg	120
cctggacagg gtcttgagtg gattggacag atttggcctg gagatgggtga tactaactac	180
aatggaaagt tcaagggtaa agccactctg actgcagacg aatcctccag cacagcctac	240
atgcaactca gcagcctagc atctgaggac tctgcggtct atttctgtgc aagacgggag	300
actacgacgg taggccgtta ttactatgct atggactact ggggccaagg gaccacggtc	360
accgtctcct ccggtgggtgg tgggttctggc ggcggcggct ccggtgggtgg tgggttctgat	420
atccagctga cccagtctcc agcttctttg gctgtgtctc tagggcagag ggccaccatc	480
tcctgcaagg ccagccaaag tgttgattat gatggtgata gttatttgaa ctggtaccaa	540
cagattccag gacagccacc caaactcctc atctatgatg catccaatct agtttctggg	600
atcccacca ggtttagtgg cagtgggtct gggacagact tcaccctcaa catccatcct	660
gtggagaagg tggatgctgc aacctatcac tgtcagcaaa gtactgagga tccgtggacg	720
ttcgggtggag ggaccaagct cgagatcaaa tccggagggtg gtggatccga cattgtactg	780
acccagtctc cagcaactct gtctctgtct ccaggggagc gtgccaccct gagctgcaga	840
gccagtcaaa gtgtaagtta catgaactgg taccagcaga agccgggcaa ggcacccaaa	900
agatggattt atgacacatc caaagtggct tctggagtcc ctgctcgctt cagtggcagt	960
gggtctggga ccgactactc tctcacaatc aacagcttgg aggctgaaga tgctgccact	1020
tattactgcc aacagtggag tagtaacccg ctcacgttcg gtggcgggac caaggtggag	1080
atcaaaggcg aaggtactag tactggttct ggtggaagtg gaggttcagg tggagcagac	1140
gacgtccaac tgggtgcagtc aggggctgaa gtgaaaaaac ctggggcctc agtgaagggtg	1200
tcctgcaagg cttctggcta cacctttact aggtacacga tgcactgggt aaggcaggca	1260
cctggacagg gtctggaatg gattggatac attaatccta gccgtgggtta tactaattac	1320

442

aatcagaagt tcaaggaccg cgtcacaatc actacagaca aatccaccag cacagcctac	1380
atggaactga gcagcctgcg ttctgaggac actgcagtct attactgtgc aagatattat	1440
gatgatcatt actgccttga ctactggggc caaggcacca cggtcaccgt ctcctca	1497

<210> 403
 <211> 499
 <212> PRT
 <213> artificial sequence

<220>

<223> CD19xVL2VH7 HLLH

<400> 403

Gln Val Gln Leu Gln Gln Ser Gly Ala Glu Leu Val Arg Pro Gly Ser	15
1 5 10	
Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Ser Ser Tyr	30
20 25	
Trp Met Asn Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile	45
35 40	
Gly Gln Ile Trp Pro Gly Asp Gly Asp Thr Asn Tyr Asn Gly Lys Phe	60
50 55	
Lys Gly Lys Ala Thr Leu Thr Ala Asp Glu Ser Ser Ser Thr Ala Tyr	80
65 70 75	
Met Gln Leu Ser Ser Leu Ala Ser Glu Asp Ser Ala Val Tyr Phe Cys	95
85 90	
Ala Arg Arg Glu Thr Thr Thr Val Gly Arg Tyr Tyr Tyr Ala Met Asp	110
100 105	
Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly	125
115 120	
Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Gln Leu Thr	140
130 135	
Gln Ser Pro Ala Ser Leu Ala Val Ser Leu Gly Gln Arg Ala Thr Ile	160
145 150 155	
Ser Cys Lys Ala Ser Gln Ser Val Asp Tyr Asp Gly Asp Ser Tyr Leu	175
165 170	
Asn Trp Tyr Gln Gln Ile Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr	190
180 185	

Asp Ala Ser Asn Leu Val Ser Gly Ile Pro Pro Arg Phe Ser Gly Ser
 195 200 205
 Gly Ser Gly Thr Asp Phe Thr Leu Asn Ile His Pro Val Glu Lys Val
 210 215 220
 Asp Ala Ala Thr Tyr His Cys Gln Gln Ser Thr Glu Asp Pro Trp Thr
 225 230 235 240
 Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Ser Gly Gly Gly Gly Ser
 245 250 255
 Asp Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
 260 265 270
 Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Tyr Met
 275 280 285
 Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr
 290 295 300
 Asp Thr Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
 305 310 315 320
 Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu
 325 330 335
 Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr
 340 345 350
 Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Gly Glu Gly Thr Ser Thr
 355 360 365
 Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Val Gln Leu
 370 375 380
 Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val
 385 390 395 400
 Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp
 405 410 415
 Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn
 420 425 430
 Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe Lys Asp Arg Val
 435 440 445
 Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser
 450 455 460

Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Tyr Tyr
 465 470 475 480

Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr
 485 490 495

Val Ser Ser

<210> 404

<211> 1497

<212> DNA

<213> artificial sequence

<220>

<223> CD19xVH7VL3 HLHL

<400> 404

caggtgcagc tgcagcagtc tggggctgag ctggtgaggc ctgggtcctc agtgaagatt	60
tcctgcaagg cttctggcta tgcattcagt agctactgga tgaactgggt gaagcagagg	120
cctggacagg gtcttgagtg gattggacag atttggcctg gagatgggtga tactaactac	180
aatggaaagt tcaagggtaa agccactctg actgcagacg aatcctccag cacagcctac	240
atgcaactca gcagcctagc atctgaggac tctgcggtct atttctgtgc aagacgggag	300
actacgacgg taggccgtta ttactatgct atggactact ggggcccaagg gaccacggtc	360
accgtctcct ccggtgggtgg tggttctggc ggcggcggct ccggtgggtgg tggttctgat	420
atccagctga ccagctctcc agcttctttg gctgtgtctc tagggcagag ggccaccatc	480
tcctgcaagg ccagccaaag tgttgattat gatgggtgata gttatttgaa ctggtaccaa	540
cagattccag gacagccacc caaactcctc atctatgatg catccaatct agtttctggg	600
atcccaccca ggtttagtgg cagtgggtct gggacagact tcaccctcaa catccatcct	660
gtggagaagg tggatgctgc aacctatcac tgtcagcaaa gtactgagga tccgtggacg	720
ttcgggtggag ggaccaagct cgagatcaaa tccggagggtg gtggatccga cgtccaactg	780
gtgcagtcag gggctgaagt gaaaaaacct ggggcctcag tgaaggtgtc ctgcaaggct	840
tctggctaca cttttactag gtacacgatg cactgggtaa ggcaggcacc tggacagggt	900
ctggaatgga ttggatacat taatcctagc cgtgggttata ctaattacaa tcagaagttc	960
aaggaccgcg tcacaatcac tacagacaaa tccaccagca cagcctacat ggaactgagc	1020
agcctgcgtt ctgaggacac tgcagtctat tactgtgcaa gatattatga tgatcattac	1080
tgccttgact actggggcca aggcaccacg gtcaccgtct cctcaggcga aggtactagt	1140
actggttctg gtggaagtgg aggttcaggt ggagcagacg acattgtact gaccagtcct	1200
ccagcaactc tgtctctgtc tccagggggag cgtgccaccc tgacctgcag agccagttca	1260

agtgaagtt acatgaactg gtaccagcag aagccgggca aggcacccaa aagatggatt 1320
 tatgacacat ccaaagtggc ttctggagtc cctgctcgct tcagtggcag tgggtctggg 1380
 accgactact ctctcacaat caacagcttg gaggtgaag atgctgccac ttattactgc 1440
 caacagtgga gtagtaaccc gctcacgttc ggtggcgagg ccaaggtgga gatcaaa 1497

<210> 405

<211> 499

<212> PRT

<213> artificial sequence

<220>

<223> CD19xVH7VL3 HLHL

<400> 405

Gln Val Gln Leu Gln Gln Ser Gly Ala Glu Leu Val Arg Pro Gly Ser
 1 5 10 15

Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Ser Ser Tyr
 20 25 30

Trp Met Asn Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile
 35 40 45

Gly Gln Ile Trp Pro Gly Asp Gly Asp Thr Asn Tyr Asn Gly Lys Phe
 50 55 60

Lys Gly Lys Ala Thr Leu Thr Ala Asp Glu Ser Ser Ser Thr Ala Tyr
 65 70 75 80

Met Gln Leu Ser Ser Leu Ala Ser Glu Asp Ser Ala Val Tyr Phe Cys
 85 90 95

Ala Arg Arg Glu Thr Thr Thr Val Gly Arg Tyr Tyr Tyr Ala Met Asp
 100 105 110

Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly
 115 120 125

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Gln Leu Thr
 130 135 140

Gln Ser Pro Ala Ser Leu Ala Val Ser Leu Gly Gln Arg Ala Thr Ile
 145 150 155 160

Ser Cys Lys Ala Ser Gln Ser Val Asp Tyr Asp Gly Asp Ser Tyr Leu
 165 170 175

Asn Trp Tyr Gln Gln Ile Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr
180 185 190

Asp Ala Ser Asn Leu Val Ser Gly Ile Pro Pro Arg Phe Ser Gly Ser
195 200 205

Gly Ser Gly Thr Asp Phe Thr Leu Asn Ile His Pro Val Glu Lys Val
210 215 220

Asp Ala Ala Thr Tyr His Cys Gln Gln Ser Thr Glu Asp Pro Trp Thr
225 230 235 240

Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Ser Gly Gly Gly Gly Ser
245 250 255

Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
260 265 270

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr
275 280 285

Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
290 295 300

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe
305 310 315 320

Lys Asp Arg Val Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr
325 330 335

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
340 345 350

Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
355 360 365

Thr Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly
370 375 380

~~Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Val Leu Thr Gln Ser~~
385 390 395 400

Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Thr Cys
405 410 415

Arg Ala Ser Ser Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro
420 425 430

Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser
435 440 445

Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser
 450 455 460 447

Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys
 465 470 475 480

Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
 485 490 495

Glu Ile Lys

<210> 406

<211> 1494

<212> DNA

<213> artificial sequence

<220>

<223> CD19xVL3VH7 LHLH

<400> 406

gatatccagc	tgacccagtc	tccagcttct	ttggctgtgt	ctctagggca	gagggccacc	60
atctcctgca	aggccagcca	aagtgttgat	tatgatggg	atagttattt	gaactggtac	120
caacagattc	caggacagcc	acccaaactc	ctcatctatg	atgcatccaa	tctagtttct	180
gggatccac	ccaggtttag	tggcagtggg	tctgggacag	acttcaccct	caacatccat	240
cctgtggaga	aggtggatgc	tgcaacctat	cactgtcagc	aaagtactga	ggatccgtgg	300
acgttcggtg	gagggaccaa	gctcgagatc	aaagggtggg	gtgggttctg	cggcggcggc	360
tccggtggg	gtgggttctca	ggtgcagctg	cagcagtctg	gggctgagct	ggtgaggcct	420
gggtcctcag	tgaagatttc	ctgcaaggct	tctggctatg	cattcagtag	ctactggatg	480
aactgggtga	agcagaggcc	tggacagggt	cttgagtggg	ttggacagat	ttggcctgga	540
gatggtgata	ctaactacaa	tggaaagtgc	aagggtaaag	ccactctgac	tgcagacgaa	600
tcctccagca	cagcctacat	gcaactcagc	agcctagcat	ctgaggactc	tgcggtctat	660
ttctgtgcaa	gacgggagac	tacgacggta	ggccggttatt	actatgctat	ggactactgg	720
ggccaagggg	ccacgggtcac	cgtctcctcc	ggagggtggg	gatccgacat	tgtactgacc	780
cagtctccag	caactctgtc	tctgtctcca	ggggagcgtg	ccaccctgac	ctgcagagcc	840
agttcaagtg	taagttacat	gaactggtac	cagcagaagc	cgggcaaggc	acccaaaaga	900
tggatttatg	acacatccaa	agtggcttct	ggagtccctg	ctcgcttcag	tggcagtggg	960
tctgggaccg	actactctct	cacaatcaac	agcttgaggg	ctgaagatgc	tgccacttat	1020
tactgccaac	agtggagtag	taaccgcctc	acgttcggtg	gcgggaccaa	ggtggagatc	1080
aaaggcgaag	gtactagtag	tgggttctgg	ggaagtggag	gttcagggtg	agcagacgac	1140

448

gtccaactgg tgcagtcagg ggctgaagtg aaaaaacctg gggcctcagt gaaggtgtcc	1200
tgcaaggctt ctggctacac ctttactagg tacacgatgc actgggtaag gcaggcacct	1260
ggacagggtc tggaatggat tggatacatt aatcctagcc gtgggttatac taattacaat	1320
cagaagttca aggaccgcgt cacaatcact acagacaaat ccaccagcac agcctacatg	1380
gaactgagca gcctgcgttc tgaggacact gcagtctatt actgtgcaag atattatgat	1440
gatcattact gccttgacta ctggggccaa ggcaccacgg tcaccgtctc ctca	1494

<210> 407

<211> 498

<212> PRT

<213> artificial sequence

<220>

<223> CD19xVL3VH7 LHLH

<400> 407

Asp Ile Gln Leu Thr Gln Ser Pro Ala Ser Leu Ala Val Ser Leu Gly
1 5 10 15

Gln Arg Ala Thr Ile Ser Cys Lys Ala Ser Gln Ser Val Asp Tyr Asp
20 25 30

Gly Asp Ser Tyr Leu Asn Trp Tyr Gln Gln Ile Pro Gly Gln Pro Pro
35 40 45

Lys Leu Leu Ile Tyr Asp Ala Ser Asn Leu Val Ser Gly Ile Pro Pro
50 55 60

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Asn Ile His
65 70 75 80

Pro Val Glu Lys Val Asp Ala Ala Thr Tyr His Cys Gln Gln Ser Thr
85 90 95

-----Glu Asp Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Gly-----
100 105 110

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Ser Gln Val
115 120 125

Gln Leu Gln Gln Ser Gly Ala Glu Leu Val Arg Pro Gly Ser Ser Val
130 135 140

Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Ser Ser Tyr Trp Met
145 150 155 160

Asn Trp Val Lys Gln Arg Pro Gly Gln Gly⁴⁴⁹ Leu Glu Trp Ile Gly Gln
 165 170 175

Ile Trp Pro Gly Asp Gly Asp Thr Asn Tyr Asn Gly Lys Phe Lys Gly
 180 185 190

Lys Ala Thr Leu Thr Ala Asp Glu Ser Ser Ser Thr Ala Tyr Met Gln
 195 200 205

Leu Ser Ser Leu Ala Ser Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg
 210 215 220

Arg Glu Thr Thr Thr Val Gly Arg Tyr Tyr Tyr Ala Met Asp Tyr Trp
 225 230 235 240

Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp
 245 250 255

Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu
 260 265 270

Arg Ala Thr Leu Thr Cys Arg Ala Ser Ser Ser Val Ser Tyr Met Asn
 275 280 285

Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp
 290 295 300

Thr Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser Gly
 305 310 315 320

Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp
 325 330 335

Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe
 340 345 350

Gly Gly Gly Thr Lys Val Glu Ile Lys Gly Glu Gly Thr Ser Thr Gly
 355 360 365

Ser Gly Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Val Gln Leu Val
 370 375 380

Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val Ser
 385 390 395 400

Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp Val
 405 410 415

Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn Pro
 420 425 430

Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe Lys Asp Arg Val Thr

435 440 450 445
 Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser Ser
 450 455 460
 Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Tyr Tyr Asp
 465 470 475 480
 Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val
 485 490 495

Ser Ser

<210> 408
 <211> 1497
 <212> DNA
 <213> artificial sequence

<220>

<223> CD19xVL3VH7 HLLH

<400> 408
 caggtgcagc tgcagcagtc tggggctgag ctggtgaggc ctgggtcctc agtgaagatt 60
 tcctgcaagg cttctggcta tgcattcagt agctactgga tgaactgggt gaagcagagg 120
 cctggacagg gtcttgagtg gattggacag atttggcctg gagatgggtga tactaactac 180
 aatggaaagt tcaagggtaa agccactctg actgcagacg aatcctccag cacagcctac 240
 atgcaactca gcagcctagc atctgaggac tctgcggtct atttctgtgc aagacgggag 300
 actacgacgg taggccgtta ttactatgct atggactact ggggccaagg gaccacggtc 360
 accgtctcct ccggtgggtgg tggttctggc ggcggcggct ccggtgggtgg tggttctgat 420
 atccagctga cccagtctcc agcttctttg gctgtgtctc tagggcagag ggccaccatc 480
 tcctgcaagg ccagccaaag tgttgattat gatggtgata gttatttgaa ctggtaccaa 540
 cagattccag gacagccacc caaactcctc atctatgatg catccaatct agtttctggg 600

 atcccacca ggtttagtgg cagtgggtct gggacagact tcaccctcaa catccatcct 660
 gtggagaagg tggatgctgc aacctatcac tgtcagcaaa gtactgagga tccgtggacg 720
 ttcggtggag ggaccaagct cgagatcaaa tccggagggtg gtggatccga cattgtactg 780
 acccagtctc cagcaactct gtctctgtct ccaggggagc gtgccaccct gacctgcaga 840
 gccagttcaa gtgtaagtta catgaactgg taccagcaga agccgggcaa ggcacccaaa 900
 agatggattt atgacacatc caaagtggct tctggagtcc ctgctcgctt cagtggcagt 960
 gggctctggga ccgactactc tctcacaatc aacagcttgg aggctgaaga tgctgccact 1020
 tattactgcc aacagtggag tagtaacctg ctcacgttcg gtggcgggac caaggtggag 1080

atcaaaggcg aaggtactag tactgggttct ggtggaagtg gaggttcagg tggagcagac 1140
 gacgtccaac tgggtgcagtc aggggctgaa gtgaaaaaac ctggggcctc agtgaagggtg 1200
 tcctgcaagg cttctggcta cacctttact aggtacacga tgcactgggt aaggcaggca 1260
 cctggacagg gtctggaatg gattggatac attaatccta gccgtgggtta tactaattac 1320
 aatcagaagt tcaaggaccg cgtcacaatc actacagaca aatccaccag cacagcctac 1380
 atggaactga gcagcctgcg ttctgaggac actgcagtct attactgtgc aagatattat 1440
 gatgatcatt actgccttga ctactggggc caaggcacca cggtcaccgt ctctca 1497

<210> 409

<211> 499

<212> PRT

<213> artificial sequence

<220>

<223> CD19xVL3VH7 HLLH

<400> 409

Gln Val Gln Leu Gln Gln Ser Gly Ala Glu Leu Val Arg Pro Gly Ser
 1 5 10 15

Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Ser Ser Tyr
 20 25 30

Trp Met Asn Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile
 35 40 45

Gly Gln Ile Trp Pro Gly Asp Gly Asp Thr Asn Tyr Asn Gly Lys Phe
 50 55 60

Lys Gly Lys Ala Thr Leu Thr Ala Asp Glu Ser Ser Ser Thr Ala Tyr
 65 70 75 80

Met Gln Leu Ser Ser Leu Ala Ser Glu Asp Ser Ala Val Tyr Phe Cys
 85 90 95

Ala Arg Arg Glu Thr Thr Thr Val Gly Arg Tyr Tyr Tyr Ala Met Asp
 100 105 110

Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly
 115 120 125

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Gln Leu Thr
 130 135 140

Gln Ser Pro Ala Ser Leu Ala Val Ser Leu Gly Gln Arg Ala Thr Ile

145	150	452 155	160
Ser Cys Lys Ala	Ser Gln Ser Val	Asp Tyr Asp Gly Asp Ser Tyr	Leu
	165	170	175
Asn Trp Tyr Gln	Gln Ile Pro Gly	Gln Pro Pro Lys Leu	Leu Ile Tyr
	180	185	190
Asp Ala Ser Asn	Leu Val Ser Gly	Ile Pro Pro Arg Phe	Ser Gly Ser
	195	200	205
Gly Ser Gly Thr	Asp Phe Thr	Leu Asn Ile His	Pro Val Glu Lys Val
	210	215	220
Asp Ala Ala Thr	Tyr His Cys Gln	Gln Ser Thr Glu	Asp Pro Trp Thr
	225	230	235
Phe Gly Gly Gly	Thr Lys Leu Glu	Ile Lys Ser Gly	Gly Gly Gly Ser
	245	250	255
Asp Ile Val Leu	Thr Gln Ser Pro	Ala Thr Leu Ser	Leu Ser Pro Gly
	260	265	270
Glu Arg Ala Thr	Leu Thr Cys Arg	Ala Ser Ser Ser	Val Ser Tyr Met
	275	280	285
Asn Trp Tyr Gln	Gln Lys Pro Gly	Lys Ala Pro Lys	Arg Trp Ile Tyr
	290	295	300
Asp Thr Ser Lys	Val Ala Ser Gly	Val Pro Ala Arg	Phe Ser Gly Ser
	305	310	315
Gly Ser Gly Thr	Asp Tyr Ser Leu	Thr Ile Asn Ser	Leu Glu Ala Glu
	325	330	335
Asp Ala Ala Thr	Tyr Tyr Cys Gln	Gln Trp Ser Ser	Asn Pro Leu Thr
	340	345	350
Phe Gly Gly Gly	Thr Lys Val Glu	Ile Lys Gly Glu	Gly Thr Ser Thr
	355	360	365
<hr/>			
Gly Ser Gly Gly	Ser Gly Gly Ser	Gly Gly Ala Asp	Asp Val Gln Leu
	370	375	380
Val Gln Ser Gly	Ala Glu Val Lys	Lys Pro Gly Ala	Ser Val Lys Val
	385	390	395
Ser Cys Lys Ala	Ser Gly Tyr Thr	Phe Thr Arg Tyr	Thr Met His Trp
	405	410	415
Val Arg Gln Ala	Pro Gly Gln Gly	Leu Glu Trp Ile	Gly Tyr Ile Asn
	420	425	430

453

Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe Lys Asp Arg Val
435 440 445

Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser
450 455 460

Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Tyr Tyr
465 470 475 480

Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr
485 490 495

Val Ser Ser

**This Page is Inserted by IFW Indexing and Scanning
Operations and is not part of the Official Record**

BEST AVAILABLE IMAGES

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images include but are not limited to the items checked:

- ☐ **BLACK BORDERS**
- ☐ **IMAGE CUT OFF AT TOP, BOTTOM OR SIDES**
- ☐ **FADED TEXT OR DRAWING**
- ☐ **BLURRED OR ILLEGIBLE TEXT OR DRAWING**
- ☐ **SKEWED/SLANTED IMAGES**
- ☐ **COLOR OR BLACK AND WHITE PHOTOGRAPHS**
- ☐ **GRAY SCALE DOCUMENTS**
- ☒ **LINES OR MARKS ON ORIGINAL DOCUMENT**
- ☐ **REFERENCE(S) OR EXHIBIT(S) SUBMITTED ARE POOR QUALITY**
- ☐ **OTHER:** _____

IMAGES ARE BEST AVAILABLE COPY.

As rescanning these documents will not correct the image problems checked, please do not report these problems to the IFW Image Problem Mailbox.